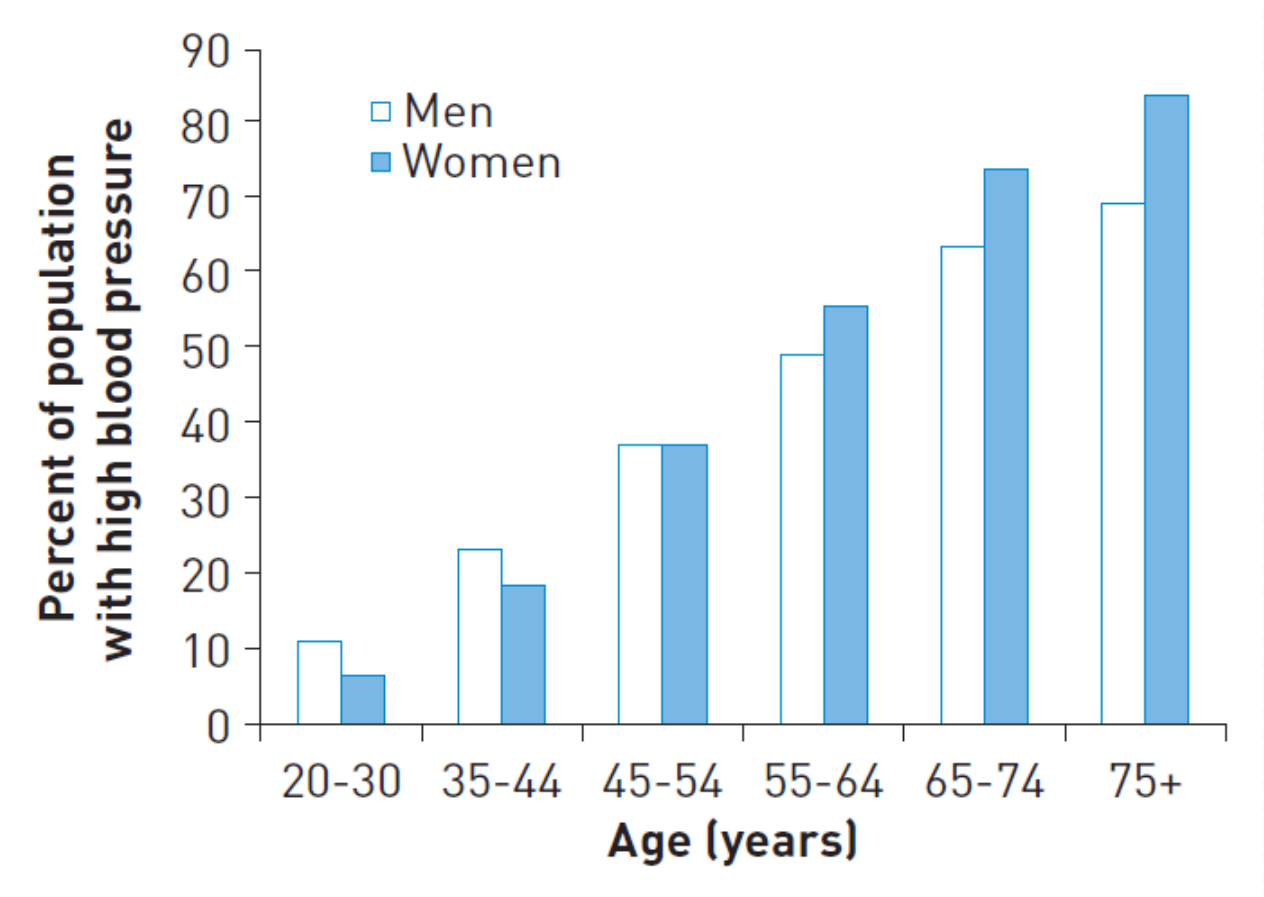
Renal denervasyon sonuçları nasıl? Farmakoterapi tekrar kazanıyor mu ?

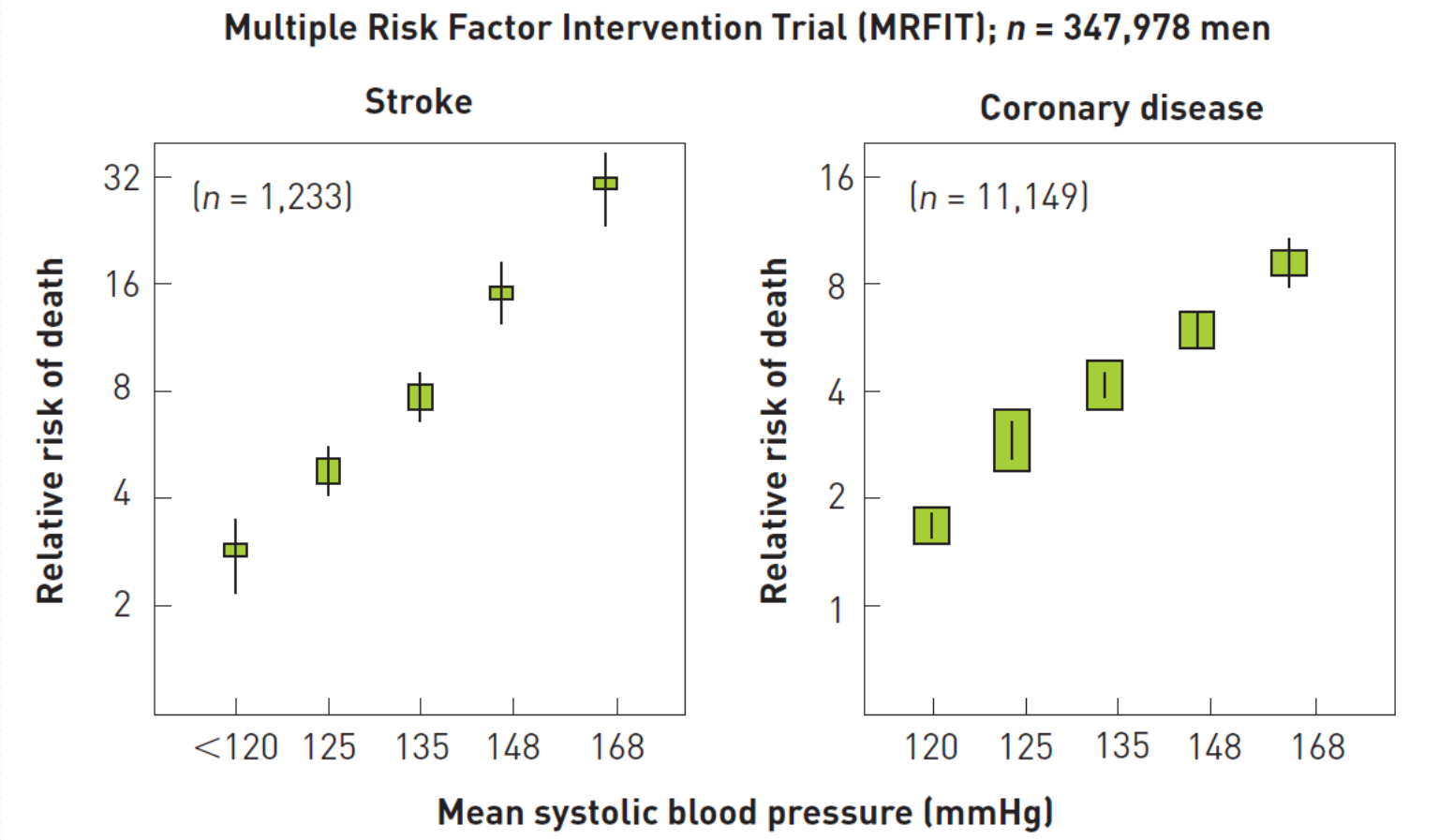
Uzm.Dr.Mustafa Ahmet HUYUT
Bezmialem Vakıf Üniversitesi
Kardiyoloji AbD.

Hipertansiyon

- En önemli kardiyovasküler ölüm nedenlerinden biri
- Yüksek tansiyon
  - İnme
  - MI
  - SVO
  - Demans
  - KBY
  - PAH



Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, Hailpern SM, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell C, Roger V, Sorlie P, Steinberger J, Thom T, Wilson M, Hong Y; American Heart Association Statistics Committee, Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008;117:e25-146.



Ruilope LM, Hypertension in 2010: Blood pressure and the kidney. Nat Rev Nephrol. 2011;7:73-4.

- Amerika Birleşik Devletleri'nin 32. başkanı Franklin Delano Roosevelt 1945 yılında hipertansiyona bağlı end organ hassarından öldüğü rapor edilmiş
- Dr raporunda ölçülen TA: 310/190 mmHg

VOLUME 27, NO. 4 MORTALITY IN SEVERE HYPERTENSION, 1944-1945

Mortality article 32711

F.D.R.'S FATAL STROKE,
MORTALITY IN SEVERE HYPERTENSION, 1944-45

Richard B Singer, MD

Hipertansiyon Nedenleri

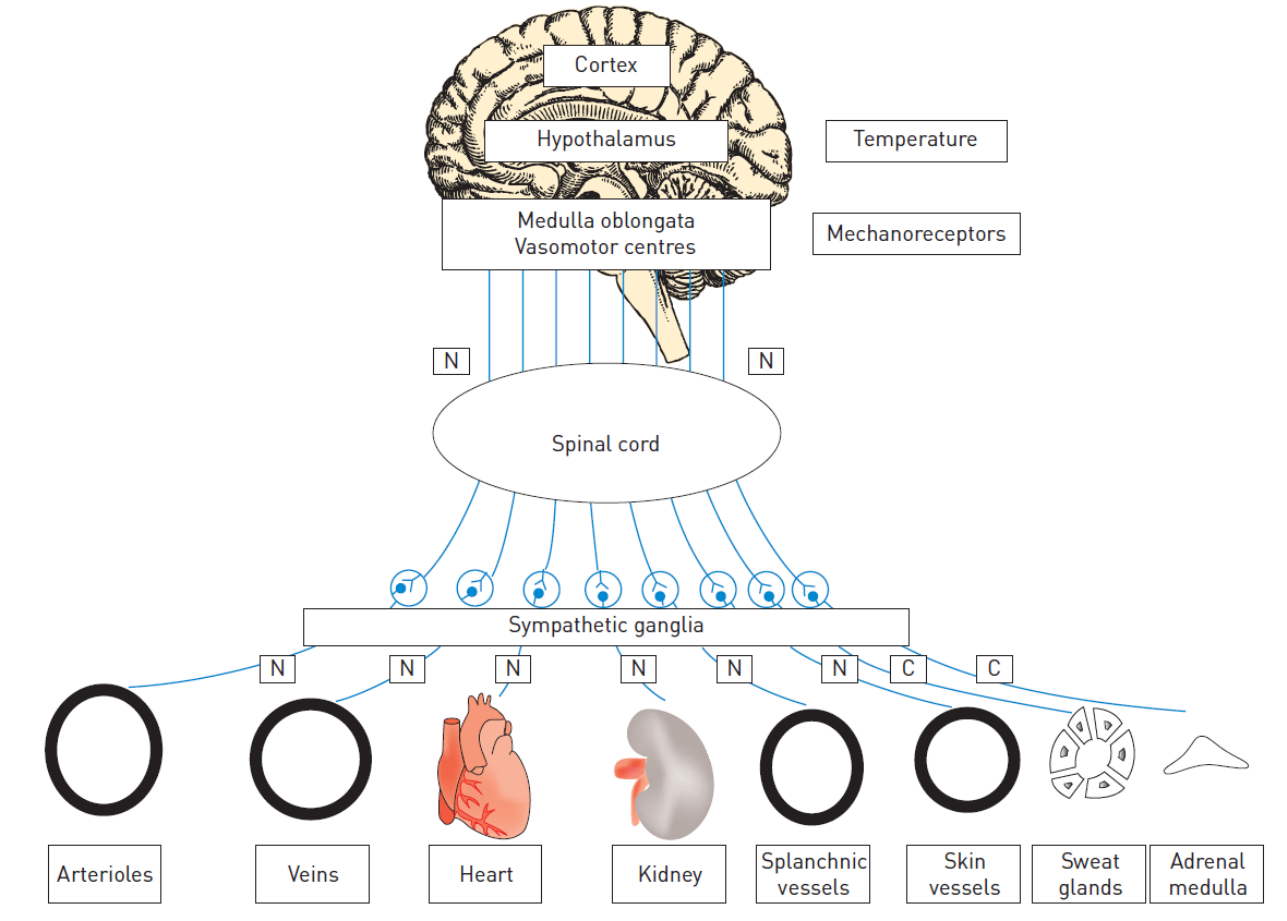
- Primer : Esansiyel Hipertansiyon: %95
- Sekonder Hipertansiyon
  - Renovasküler Hipertansiyon
    - Renal Arter Stenozu, Fibromüsküler Displazi (FMD; aterosklerotik renal arter stenozunun aksine, klasik olarak, renal arterin orta ve distal üçte ikisini tutar. Ayrıca renal arter dallarını da tutabilir.)
  - Renal Parankimal Hastalıklar
    - Diabetik yada kronik glomerulonefrit,
  - Endokrin Hastalıklar
    - Conn Sendromu
    - Feokromasitoma
    - Cushing Sendromu
    - Hipotiroidizm, Hipertiroidizm, Hiperparatiroidizm
  - Aort koarktasyonu
  - Akromegali
  - Uyku apne sendromu
  - İlaçlar (Oral kontraseptif, NSAİ, Kortikosteroidler)

Renal Denervasyon

- Endikasyonları
  - Tedaviye dirençli hipertansiyon: biri diüretic olmak üzere en az 3 tolere edilebilen yüksek doz antihipertansif alan
  - Ofis SBP ≥160 mmHg (Tip II diabetli olgularda ≥150 mmHg)
  - GFR>45 ml/dk
  - Sekonder seberler dışlanmış
  - Renal arter stenozu olmayan yada daha önce renal invaziv işlem geçirme öyküsü olmayan
  - Renal arter çapı ≥4mm, Uzunluğu ≥ 20 mm olmalı,
  - Tercihan aksesuar renal arteri olmayan
  - Pseudorezistans dışlanmış: Beyaz önlük etkisi, yanlış ölçüm, uygunsuz tedavi, hasta uyumsuzluğu (ABPM kullanılmış).

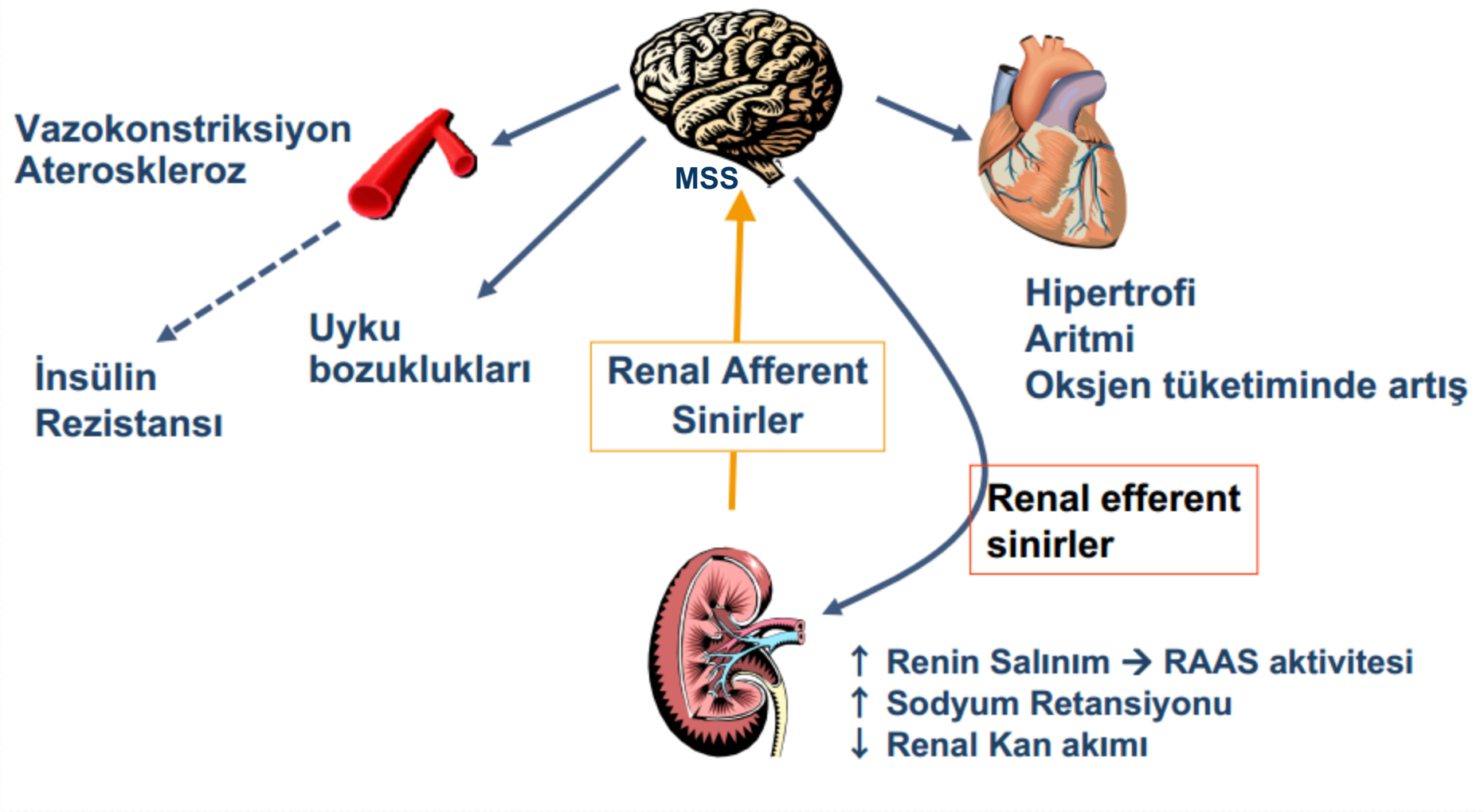
The Joint UK Societies' Consensus Statement on Renal Denervation for Resistant Hypertension. 26th January 2012 - http://guidance.nice.org.uk/IPG418

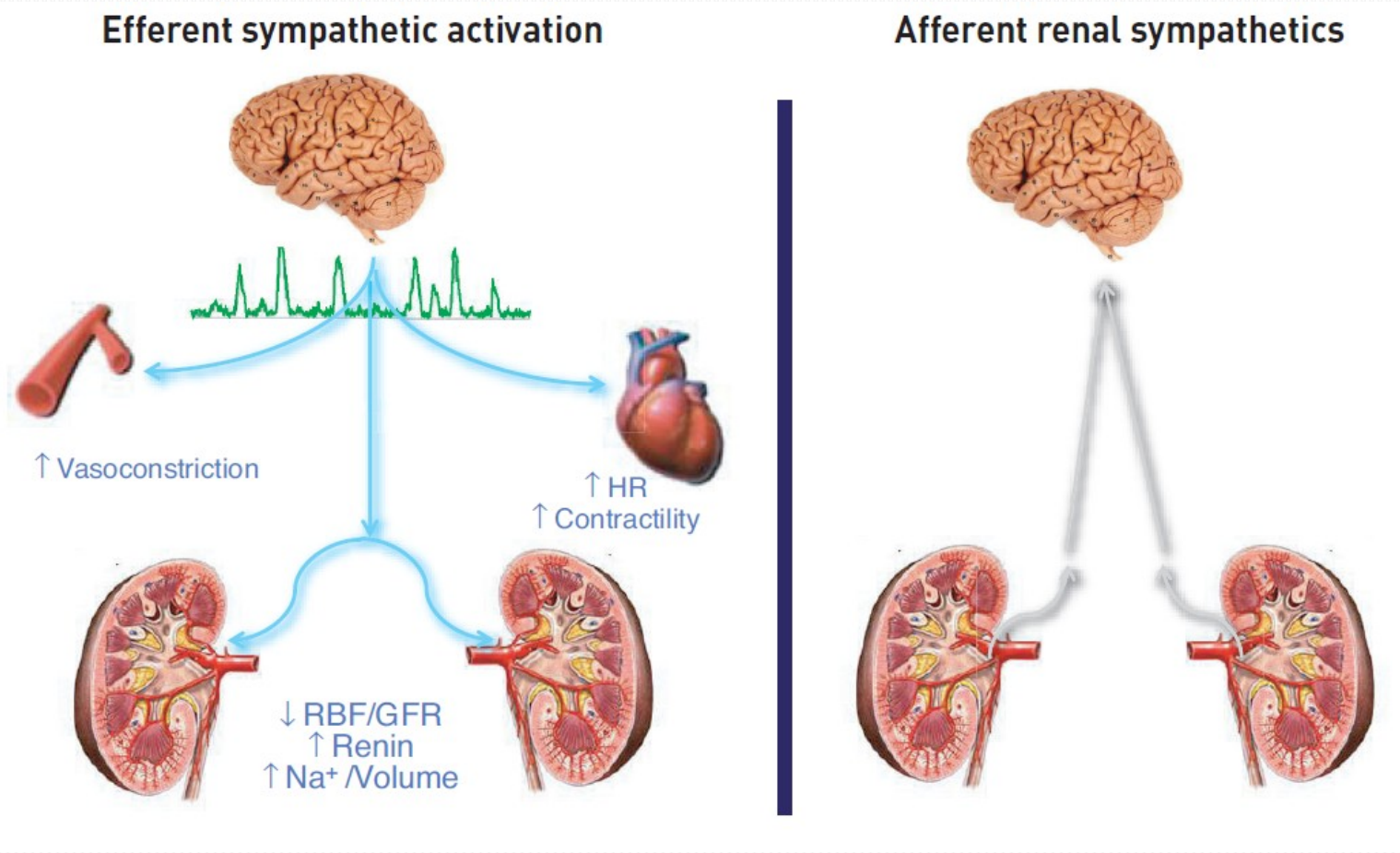
Sempatik SS



Shepherd JT, Vanhoutte PM. Local modulation of adrenergic neurotransmission in blood vessels. *J Cardiovasc Pharmacol.* 1985;7:S167-78.

Renal Sempatik Efferent ve Afferent Sinirler:
(Böbrek, santral sempatik uyarı oluşumunda merkez işlevi görür)



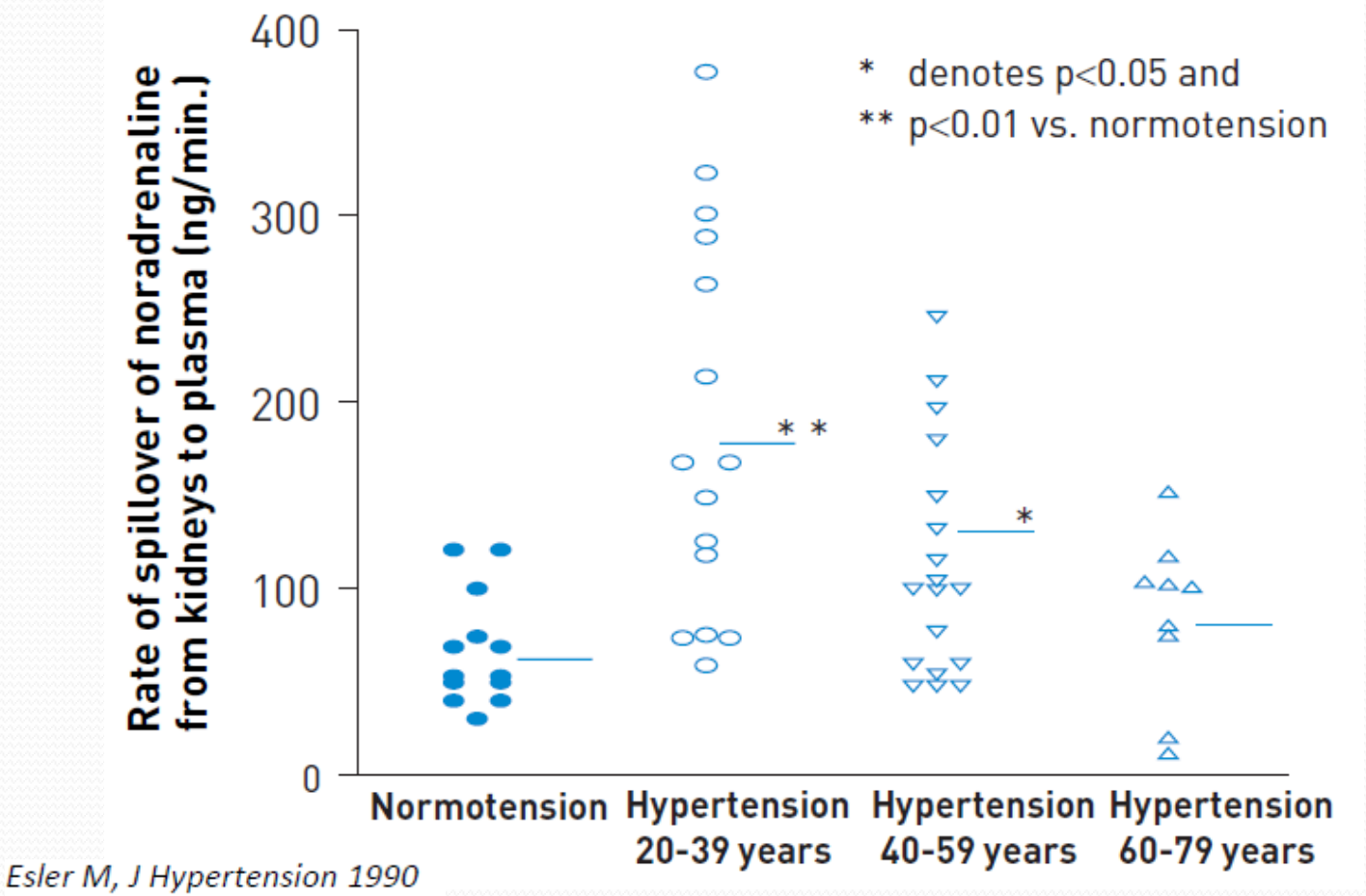


↓ RBF: Renal Blood Flow(Renal kan akımı)

Sempatik sinir sistemi jukstaglomerüler aparattan renin salınımını artırır.

DiBona GF. Functionally specific renal sympathetic nerve fibers: role in cardiovascular regulation. *Am J Hypertens.* 2001;14:163S-170S.

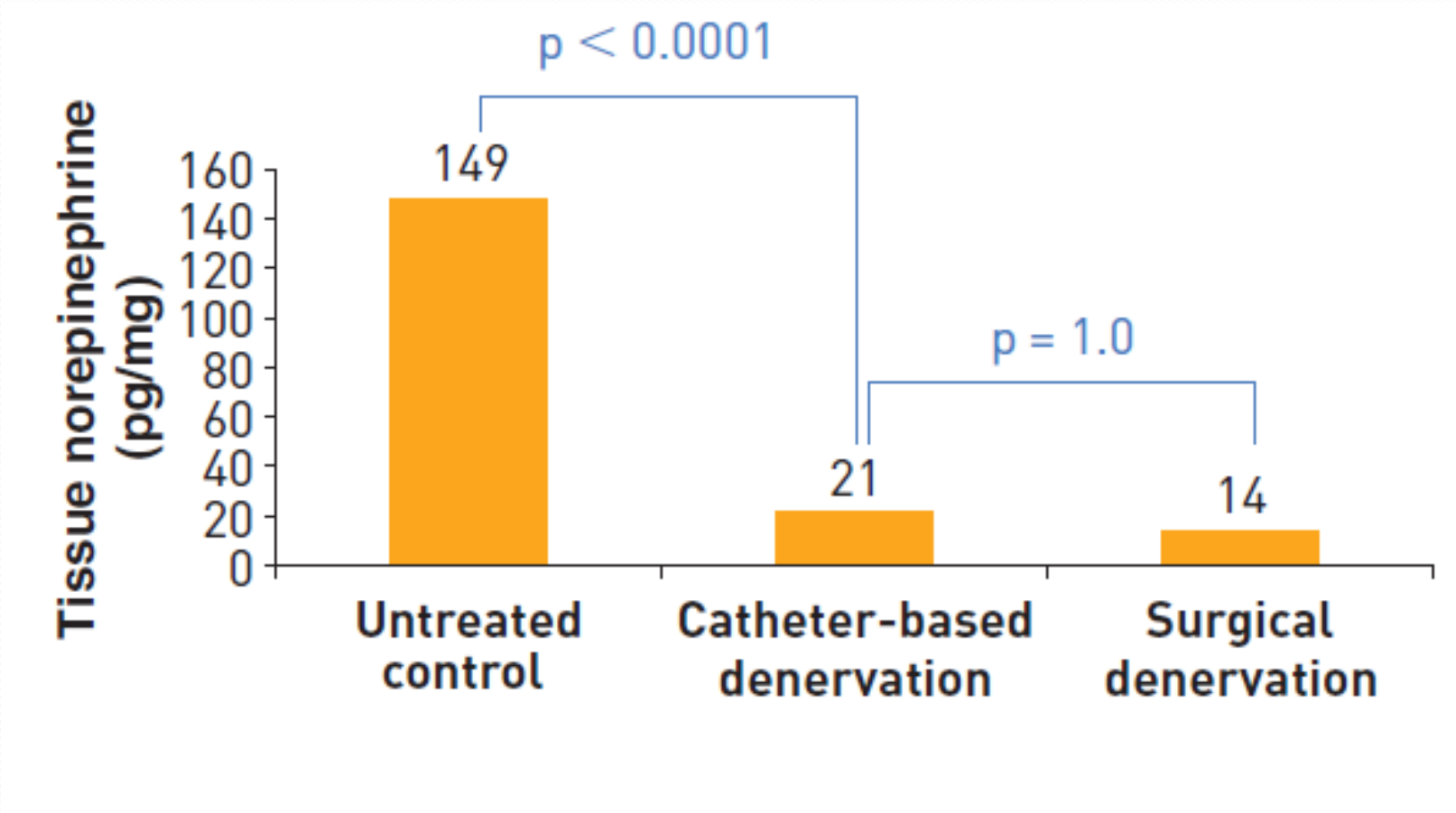
Plazma Norepinefrin Salınım Düzeyleri



Esler M, J Hypertension 1990

Allen EV. Sympathectomy for essential hypertension. *Circulation*. 1952:6:131-40.
Smithwick RH. Sympathectomy, splanchniecoctomy and vagotomy. *Rev Surg*. 1973;30:153-73.

Sempatik Denervasyon



Schlaich, MP, Sobotka PA, Krum H, Lambert E, Esler MD. Renal sympathetic-nerve ablation for uncontrolled hypertension. N Engl J Med. 2009;361:932-4. .

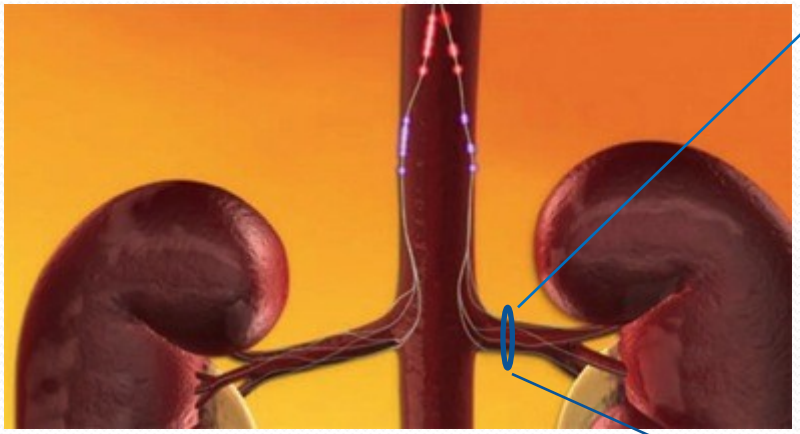
Renal Denervasyon

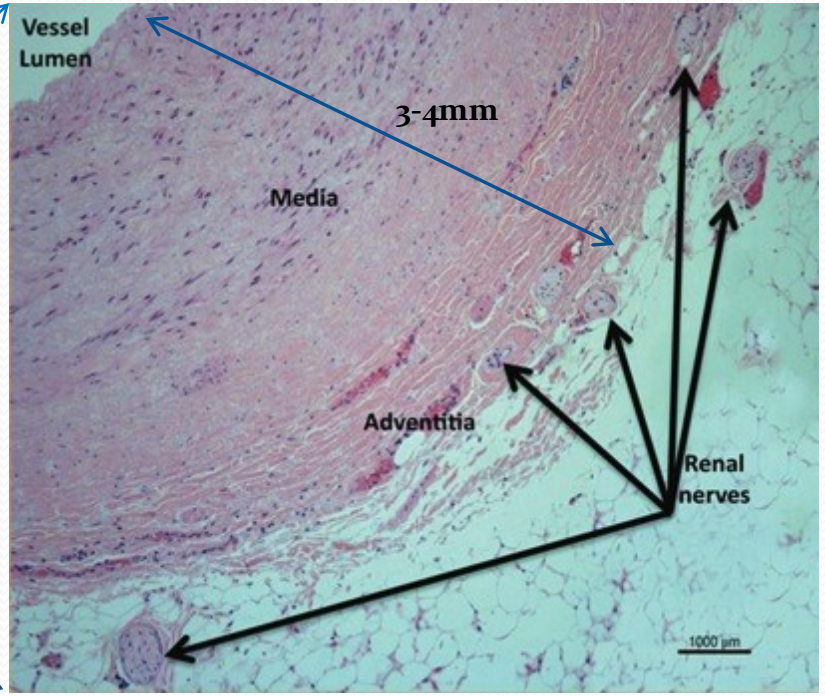
- Cerrahi sempatektomi,1950'li yıllarda radikal cerrahi sempatektomi (splanknikektomi)
    - Kan basıncında ciddi düşüşler var.
    - Yan etkiler; Ortostatik taşikardi, postüral hipotansiyon erektil disfonksiyon, mesane ve barsak sorunları
- Renal arterin kesilmesi ve reanastomozu
- Lokal fenol uygulaması ile adventisyanın hasarlanması
- Renal sempatik sinir radyofrekans ablasyonu

Renal Denervasyon

Amaç:

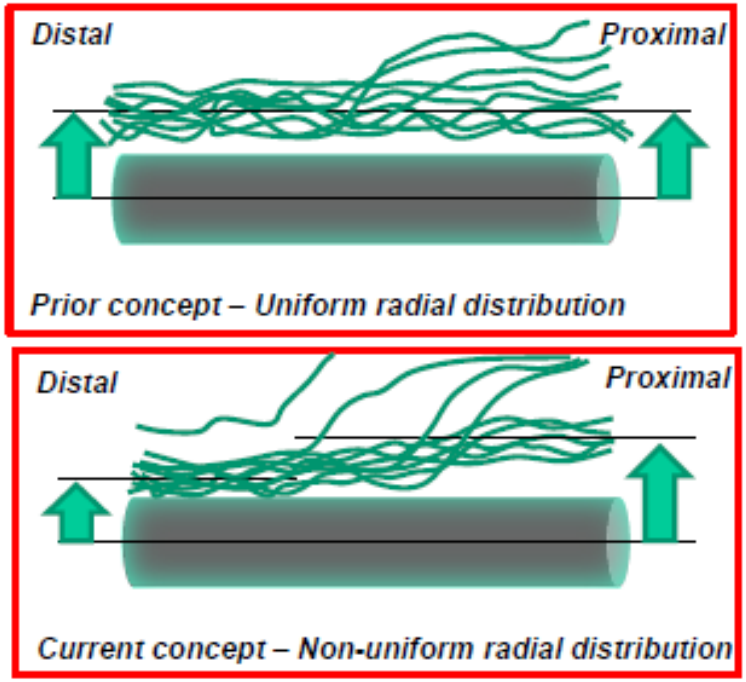
- Renal arter adventisyası içinde yer alan sempatik afferent ve efferent sinirlerin ablasyonu ile sempatik aktivasyonun baskılanması.

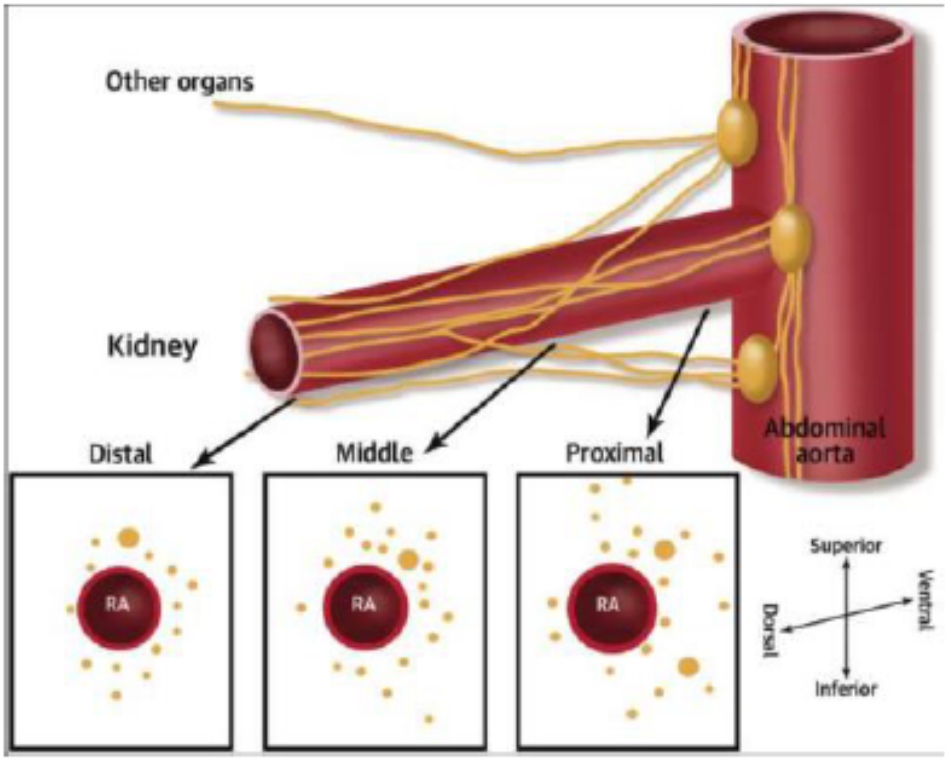




4 Hafta süreyle aspirin kullanımı önerilmekte

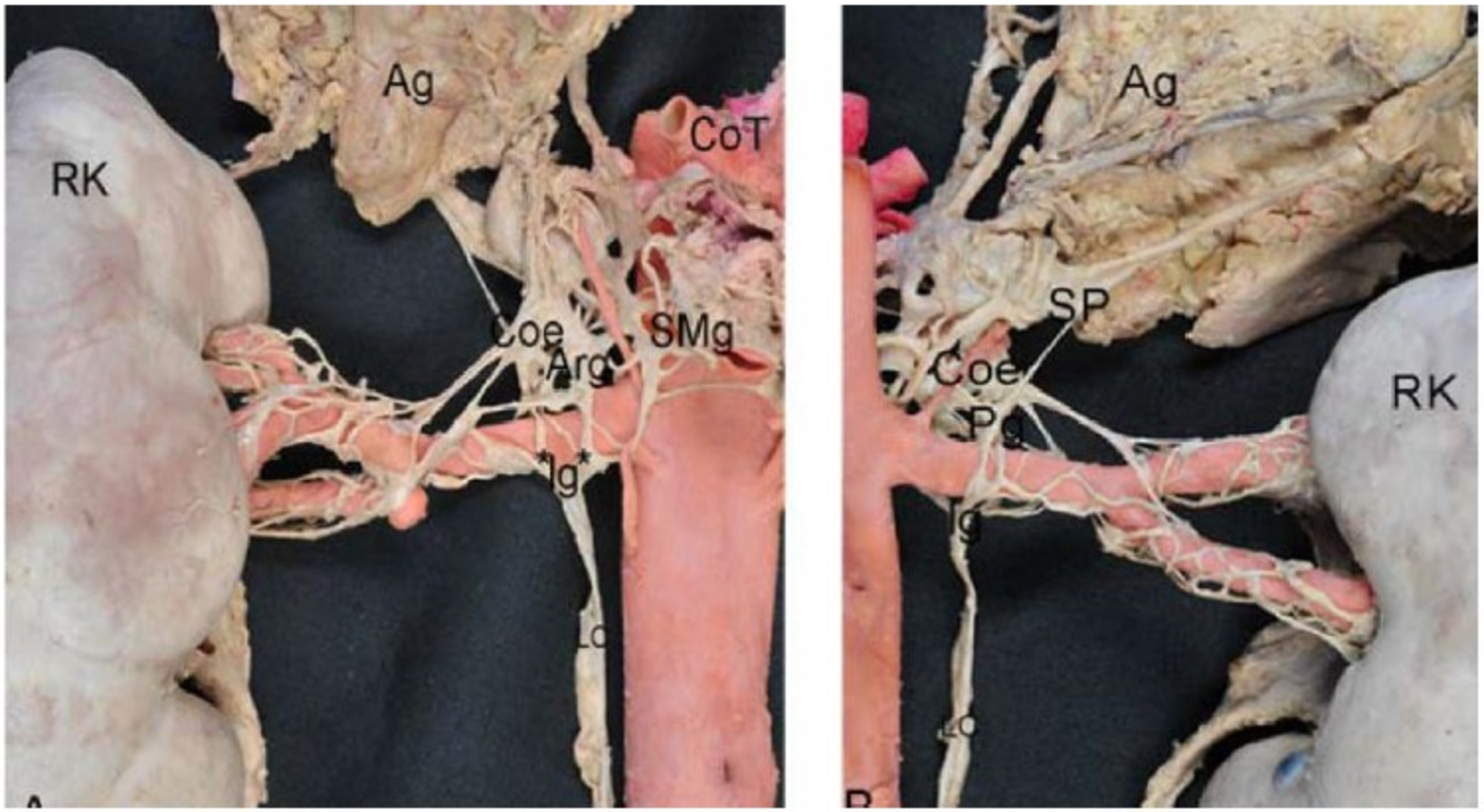
Today we know that distal nerves are more close to the vessel than proximal nerves





Sakakura K et al. J Am Coll Cardiol. 2014

Evolving Perspective on Renal Nerve Distribution: Anatomic Data Regarding Extent of Innervation

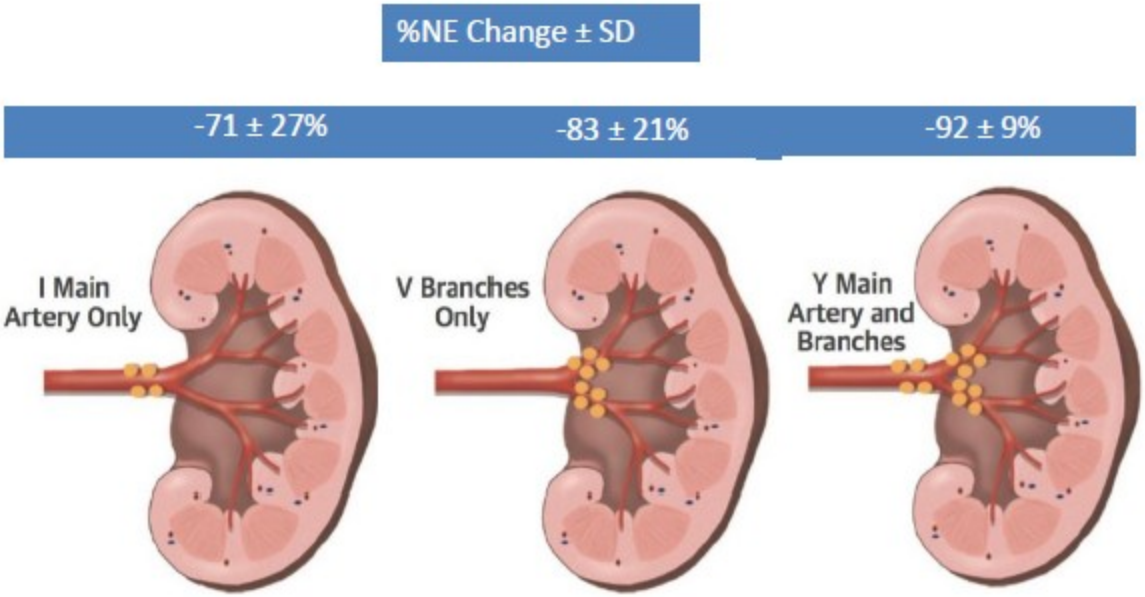


Mompeo et al., *Clin Anat*, 2016 doi: 10.1002/ca.22720

Imndaze et al. *J Interv Cardiol*. 2016 Sep 29. doi: 10.1111/joic.12343

Piedmont HEART

Combined Branch and Main Artery Treatment Resulted in Greater and More Consistent Pre-Clinical Effect

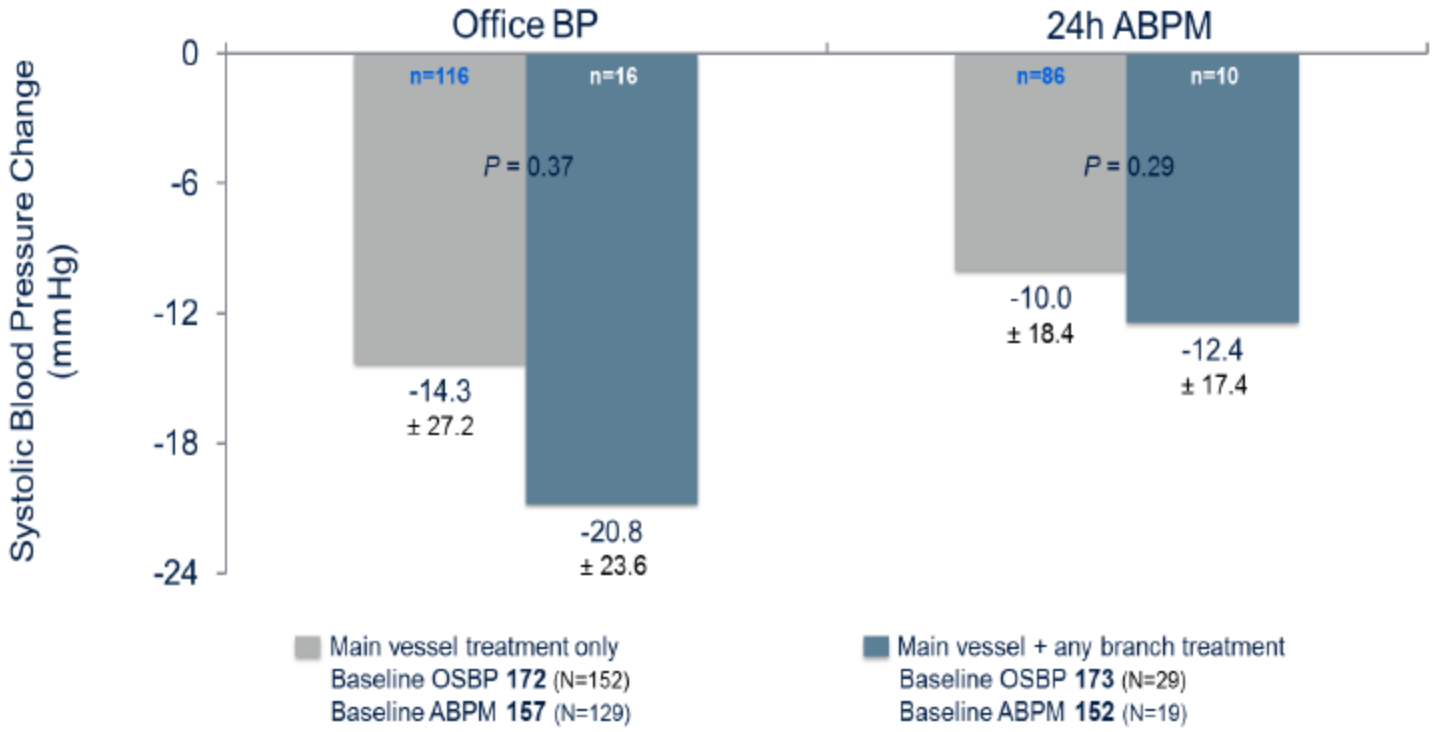


Pre-clinical data show significantly greater reductions in renal sympathetic activity with combined proximal and distal therapy application.

Mahfoud et al. *J Am Coll Cardiol*. 2015;66:1766-75.

Piedmont HEART

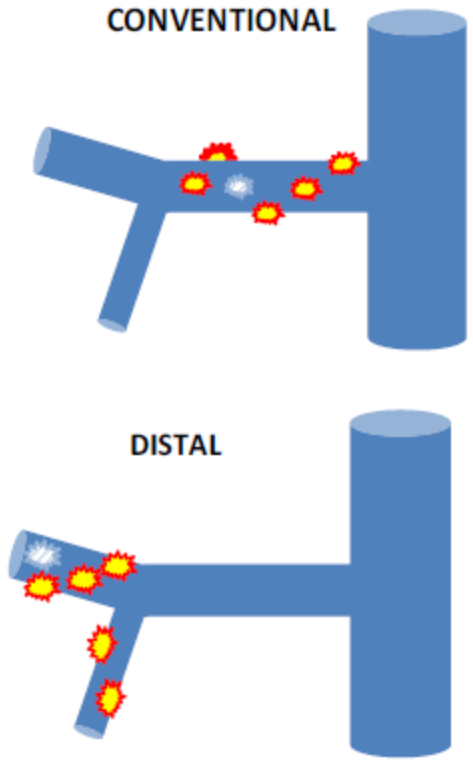
GLOBAL SYMPLICITY REGISTRY:
Subset: Renal Artery Branch Treatment with Spyral at 6 months

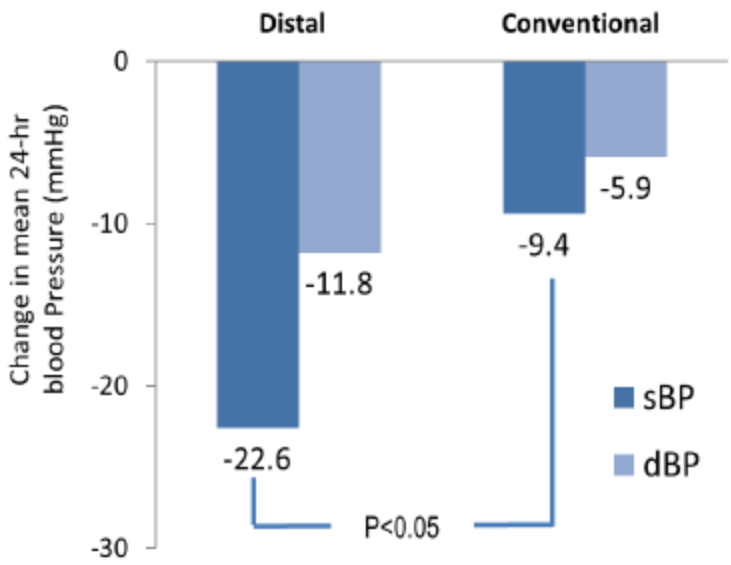


Mahfoud, EuroPCR, 2016

Piedmont HEART

Greater Decreases in Ambulatory Blood Pressure with Distal vs. Proximal RDN Therapy Application in Treatment Resistant Hypertensive Patients



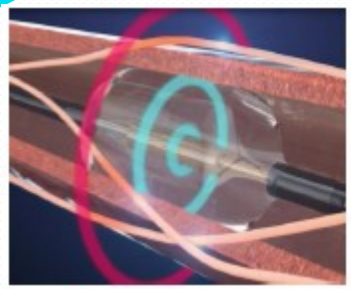


N=51

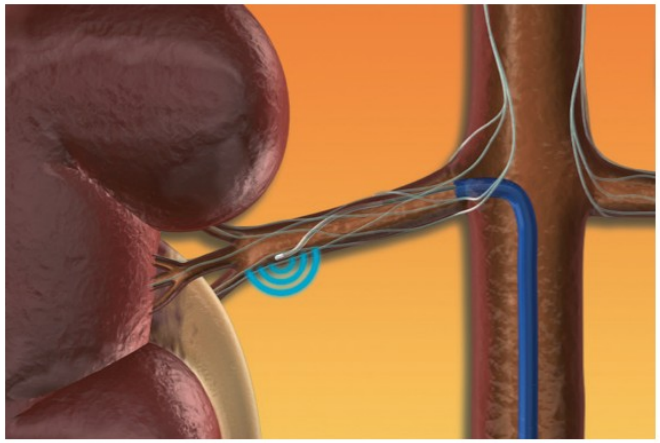
6 month change in BP with Symplicity Flex

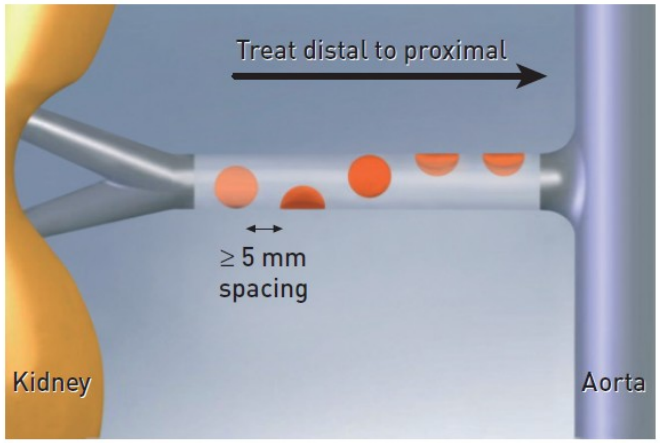
Pekarskiy EuroPCR, 2016

Piedmont HEART

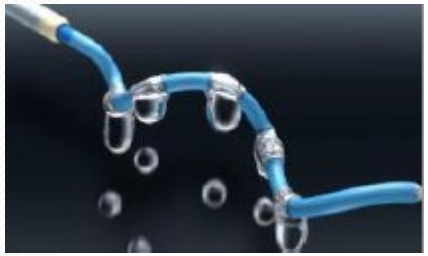


Paradise Ultrasound

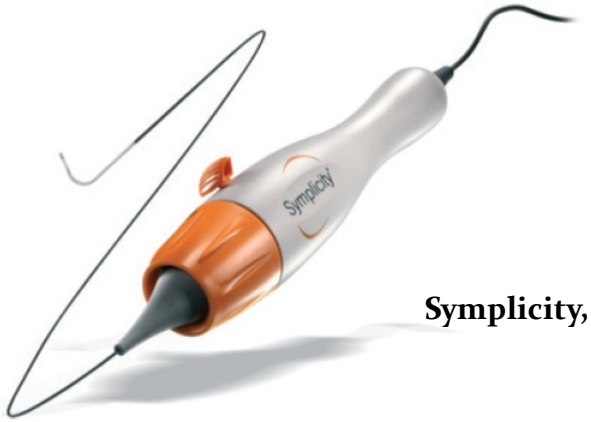




EnligHTN, St.Jude

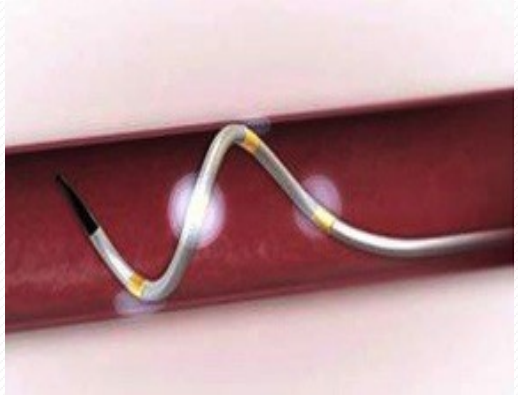


Cordis ThermoCool



Symplicity, Ardian, Medtronic

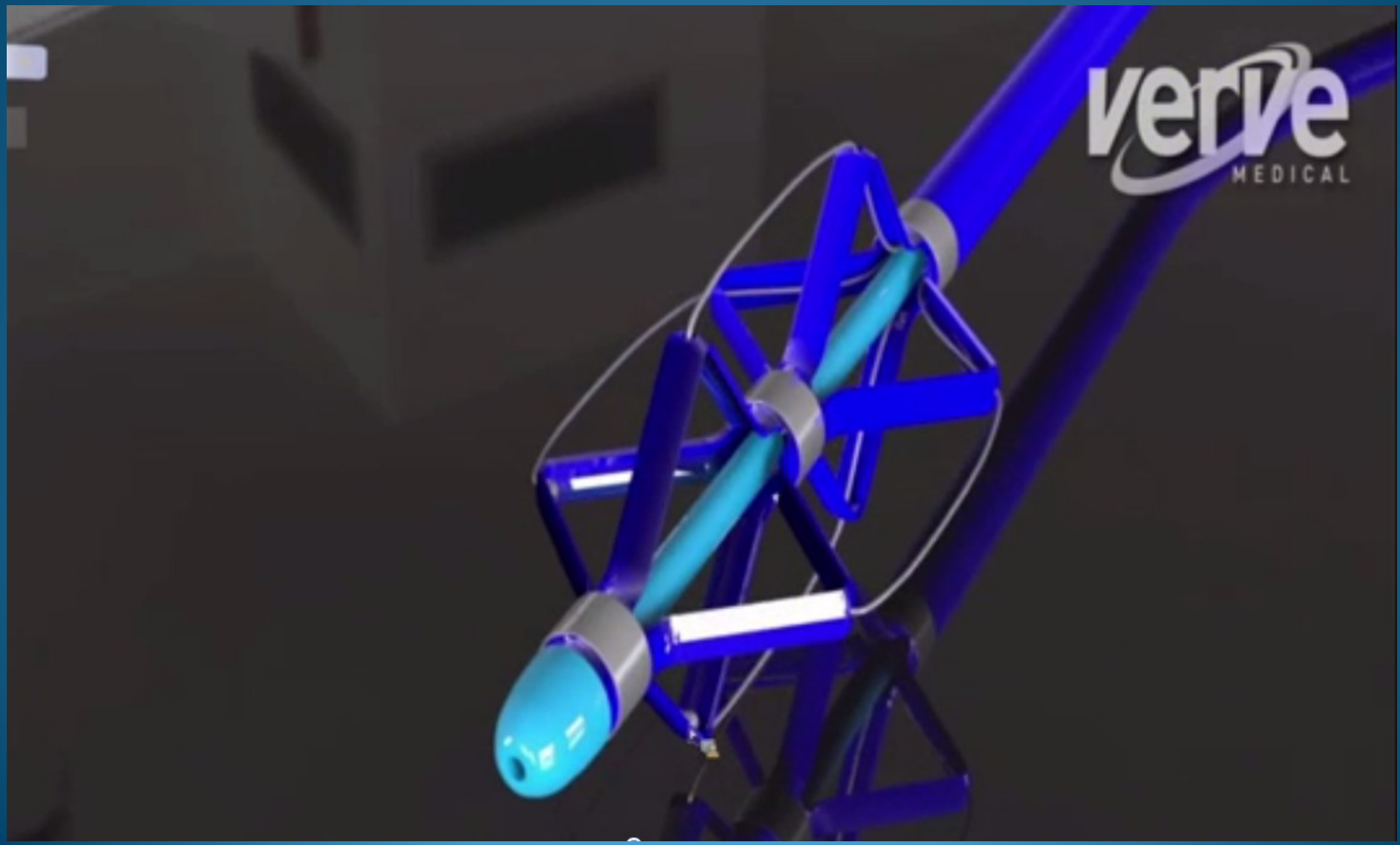
Vessix, Boston



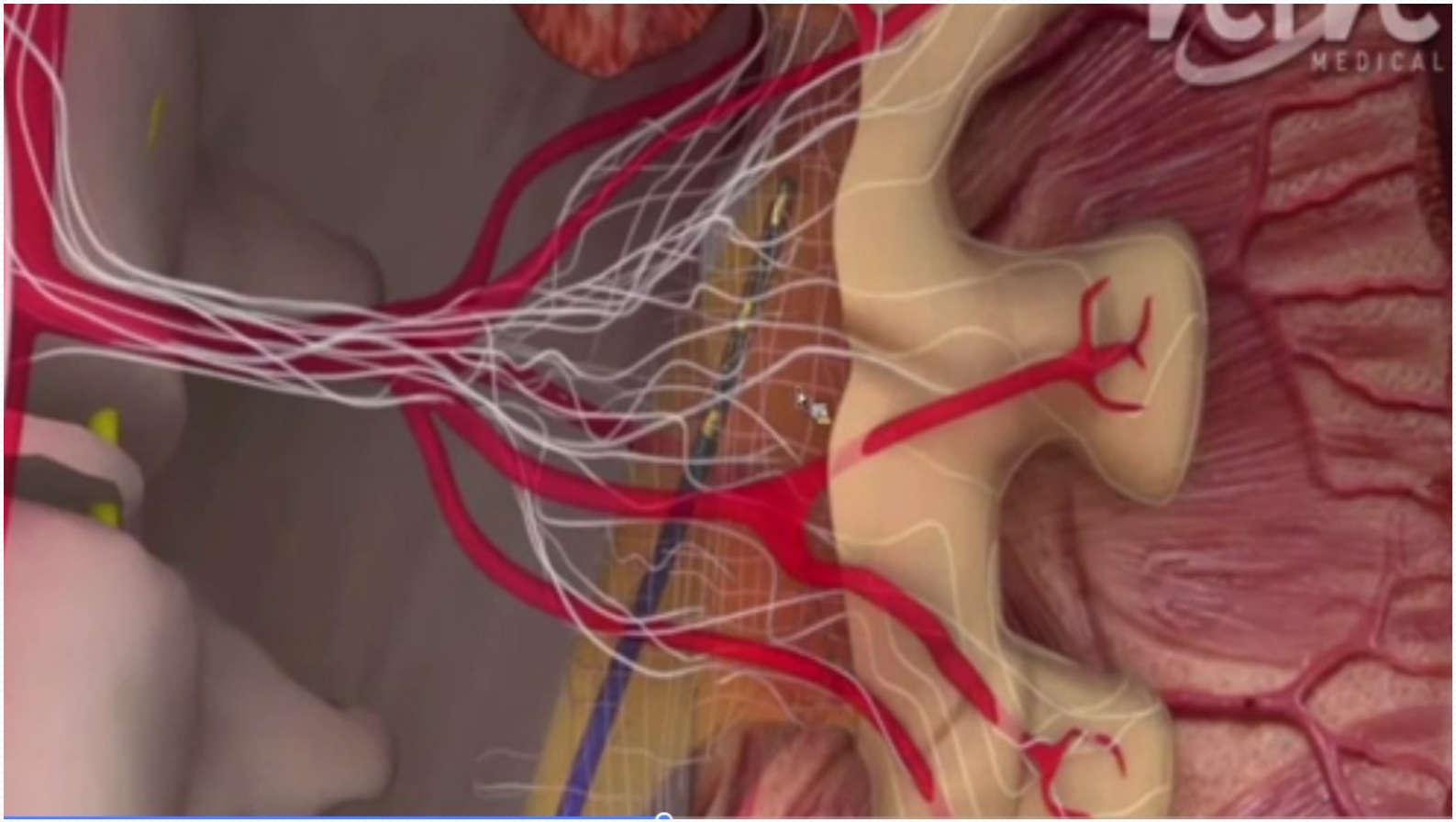
Spyral system multi-electrode catheter

PeriVascular Renal Denervation

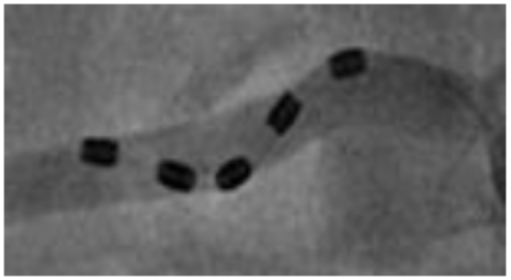
Transuretral Yaklaşım,Verve Medical

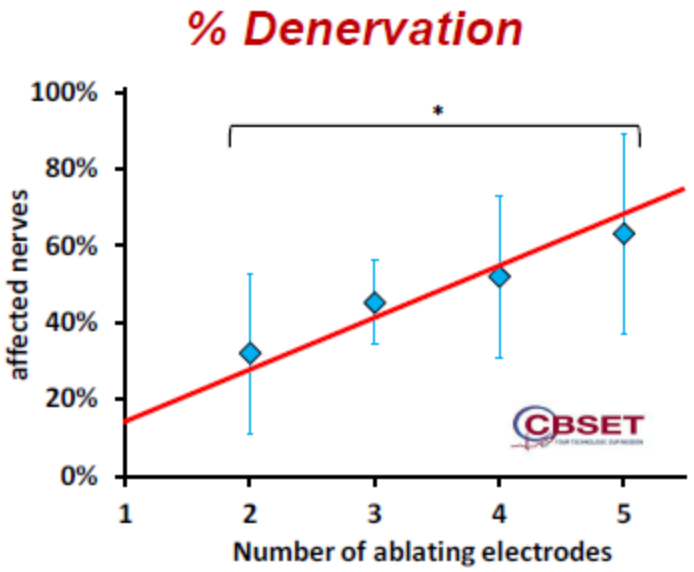


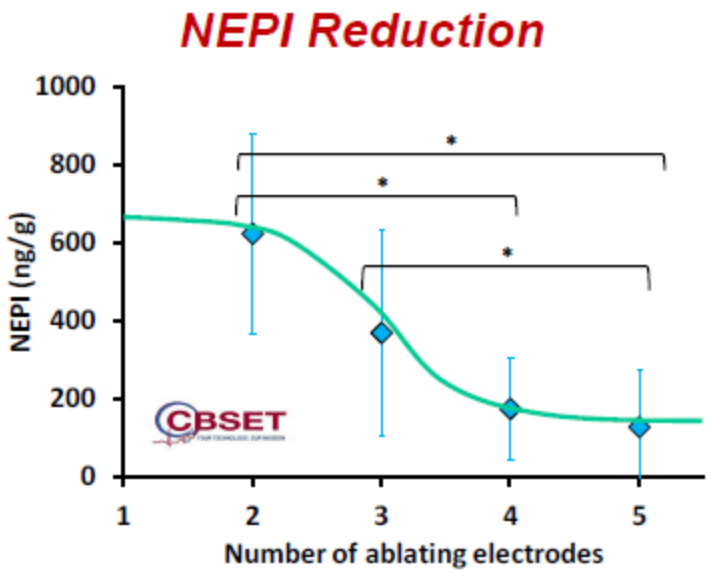
Transuretral Yaklaşım



More helical electrodes cause more denervation and more Norepinephrine reduction

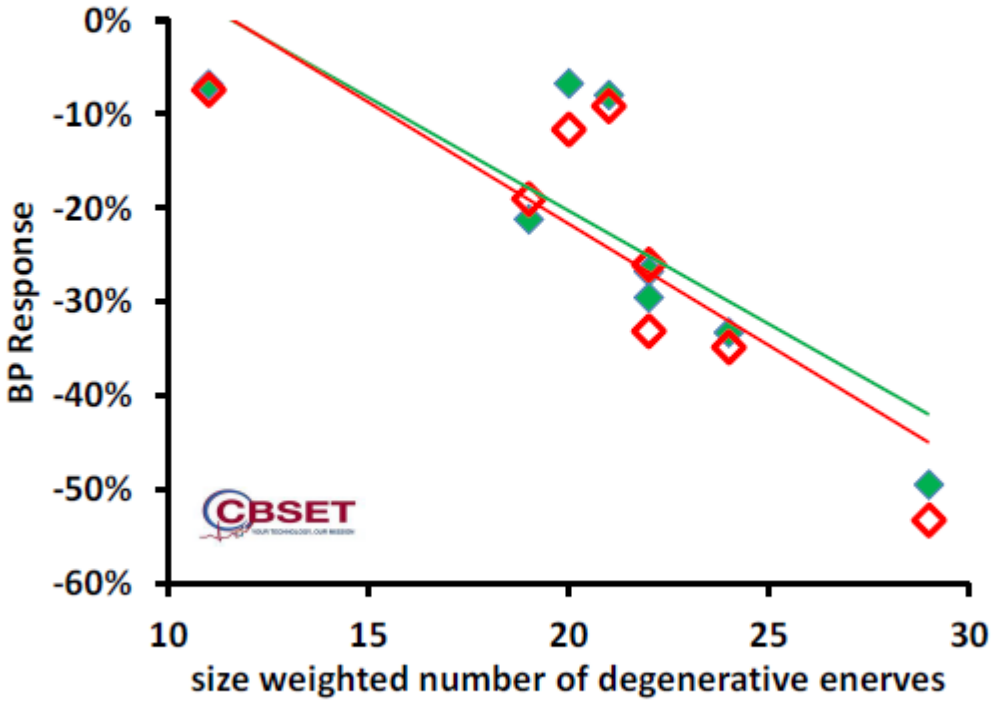






Tzafriri et al Sci Transl Med 2015

More denervation causes more blood pressure reduction



Tzafriri et al Sci Transl Med 2015

Unilateral Renalane RDN
5-electrode treatments: 9 to 10W/60 sec

Ardian, Medtronic

- Monopolar
- Tek elektrod
- 6F Kılavuz kateter
- 8W
- 2dk'lık RF periyodu x ~5
- ≥ 4mm arterlerde
- **~20dk**

EnligHTN, St.Jude

- Monopolar
- Dört elektrod (1cm)
- **8F** Kılavuz kateter
- 6W
- 1.5dk'lık RF periyodu x 2-3
- ≥ 4mm arterlerde
- ~10dk

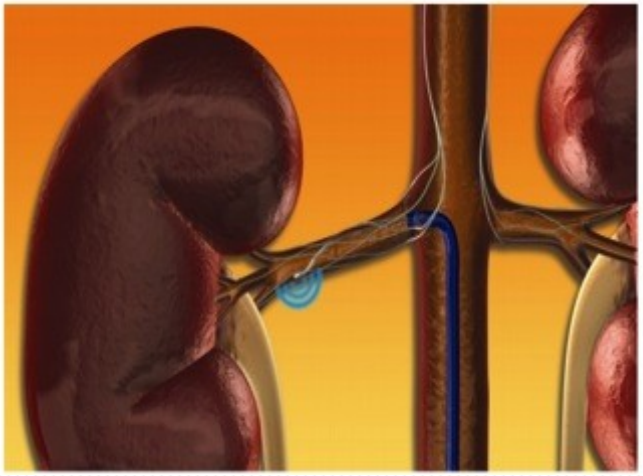
Vessix, Boston

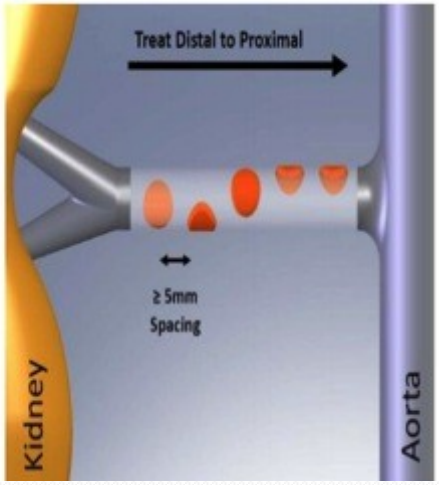
- **Bipolar**
- Sekiz elektrod (2cm)
- 6F Kılavuz kateter
- **1-2W**
- **30sn** RF periyodu x 1-2
- ↓ **4mm** arterlerde
- ~2dk

Radiofrequency ablation	Symplicity	Single electrode and Spyral™-Multielectrode catheter
	EnligHTN	Multielectrode catheter
	Vessix V2	Balloon-mounted catheter
	Renlane	Irrigated multi-electrode catheter
	ThermoCool	Cryoablative irrigated catheter
	Chilli II	Cryoablative irrigated catheter
Ultrasound ablation	Paradise	Ultrasound catheter
	TIVUS	Ultrasound catheter under development
	KONA medical	Ultrasound catheter under development
Pharmacological ablation	Bullfrog microinfusion	Microneedle-equiped balloon catheter

- Denervasyon kateteri segmental arter ayrımına kadar ilerletilir.

- Segmental arter ayrımı öncesinden, orifise kadar 5mm aralıklarla, helikal konumlandırılarak 2'şer dk süreyle ablasyon uygulanır.

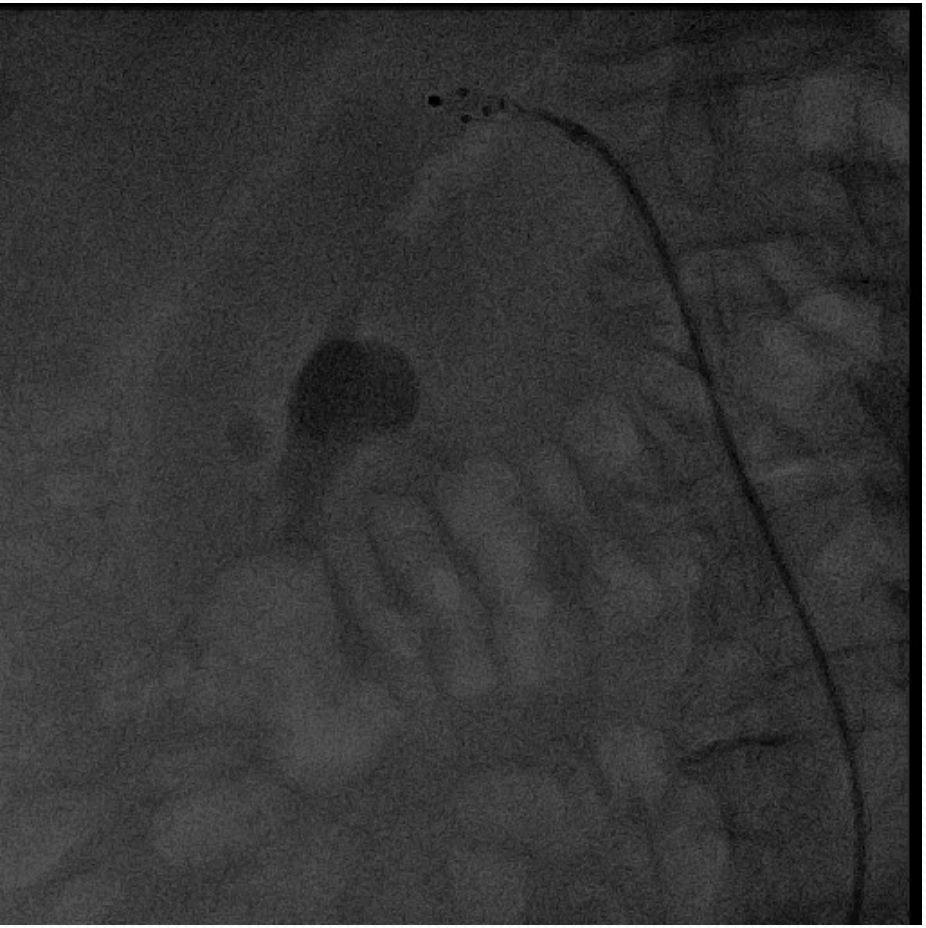


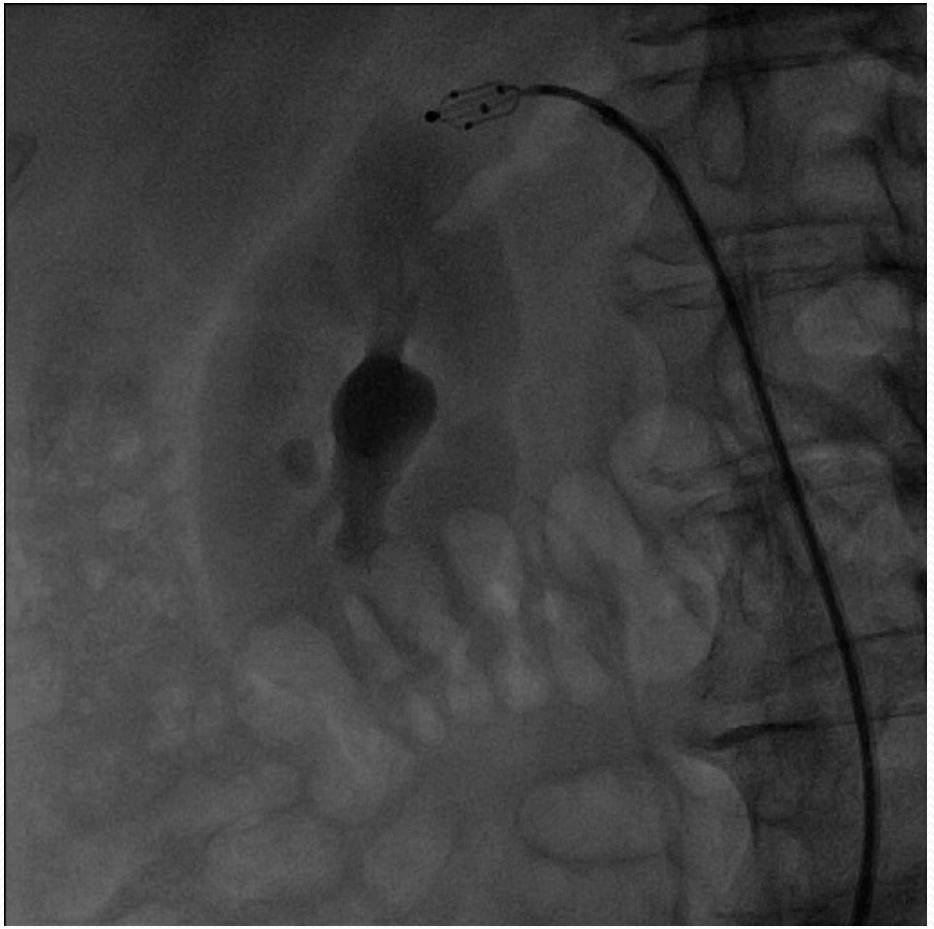


Kliniğimizde Yapılan Denervasyon Örneği

- RF ablasyonu
- Renal arter orifisi düzeyinde, üst duvar ablasyonu
- İşlem sırasında ve sonrasında kontrol anjiografi (Spazm, Diseksiyon, Rüptür açısından)
- 4 Hafta süreyle aspirin

EnligHTN, St.Jude





Renel Denervasyon Çalışmaları

European Heart Journal (2013) 34, 2159–2219
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Authors/Task Force Members: Giuseppe Mancia (Chairperson) (Italy)*, Robert Fagard (Chairperson) (Belgium)*, Krzysztof Narkiewicz (Section co-ordinator) (Poland), Josep Redon (Section co-ordinator) (Spain), Alberto Zanchetti (Section co-ordinator) (Italy), Michael Böhm (Germany), Thierry Christiaens (Belgium), Renata Cifkova (Czech Republic), Guy De Backer (Belgium), Anna Dominiczak (UK), Maurizio Galderisi (Italy), Diederick E. Grobbee (Netherlands), Tiny Jaarsma (Sweden), Paulus Kirchhof (Germany/UK), Sverre E. Kjeldsen (Norway), Stéphane Laurent (France), Athanasios J. Manolis (Greece), Peter M. Nilsson (Sweden), Luis Miguel Ruilope (Spain), Roland E. Schmieder (Germany), Per Anton Sirnes (Norway), Peter Sleight (UK), Margus Viigimaa (Estonia), Bernard Waeber (Switzerland), Faiez Zannad (France)

- Renal denervasyon klavuzda IIb C

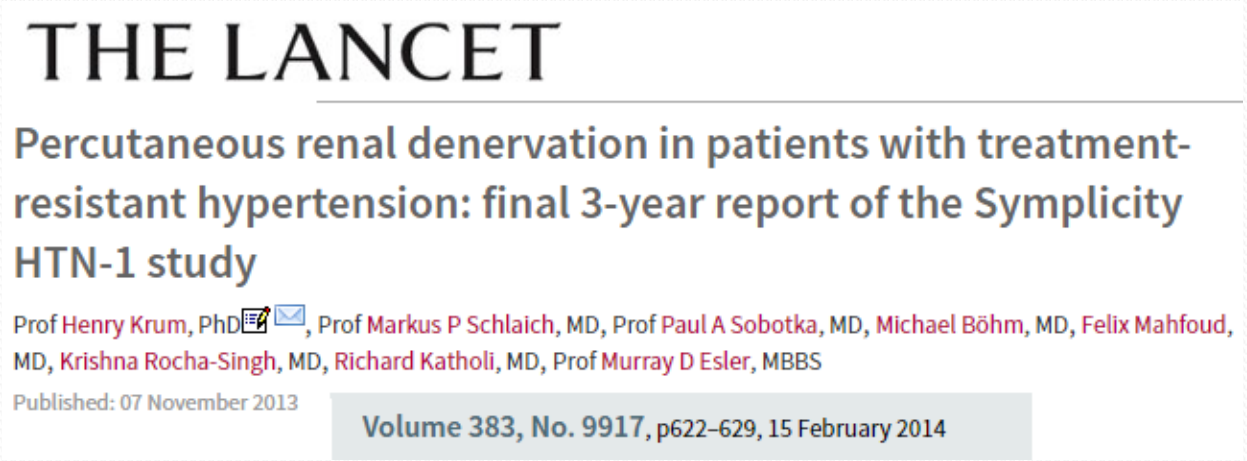
Therapeutic strategies in patients with resistant hypertension

Recommendations	Class [a]	Level [b]	Ref. [c]
In resistant hypertensive patients it is recommended that physicians check whether the drugs included in the existing multiple drug regimen have any BP lowering effect, and withdraw them if their effect is absent or minimal.	I	C	-
Mineralocorticoid receptor antagonists, amiloride, and the alpha-1-blocker doxazosin should be considered, if no contraindication exists.	IIa	B	604, 606, 607, 608
[redacted] and [redacted] may be considered.	IIb	C	-
Until more evidence is available on the long-term efficacy and safety of renal denervation and baroreceptor stimulation, it is recommended that these procedures remain [redacted] and diagnosis and follow-up restricted to hypertension centers.	I	C	-
It is recommended that the invasive approaches are considered only for truly resistant hypertensive patients, with clinic values ≥160 mmHg SBP or ≥110 mmHg DBP and with BP elevation confirmed by ABPM.	I	C	-

ABPM = ambulatory blood pressure monitoring; BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendation(s).

Symplicity HTN-1

- 153 hasta dahil edilmiş fakat 3 yıllık takipte kayıplar ile toplamda 88 hasta verisi elde edilmiş
- Ortalama yaş 57
- 3 yıllık takipte, her 6 ayda bir kontrol
- Hastaların %28 tip 2 diabetes mellitus



THE LANCET

Percutaneous renal denervation in patients with treatment-resistant hypertension: final 3-year report of the Symplicity HTN-1 study

Prof Henry Krum, PhD, Prof Markus P Schlaich, MD, Prof Paul A Sobotka, MD, Michael Böhm, MD, Felix Mahfoud, MD, Krishna Rocha-Singh, MD, Richard Katholi, MD, Prof Murray D Esler, MBBS

Published: 07 November 2013

Volume 383, No. 9917, p622–629, 15 February 2014

Symplicity HTN-1

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Published: 07 November 2013

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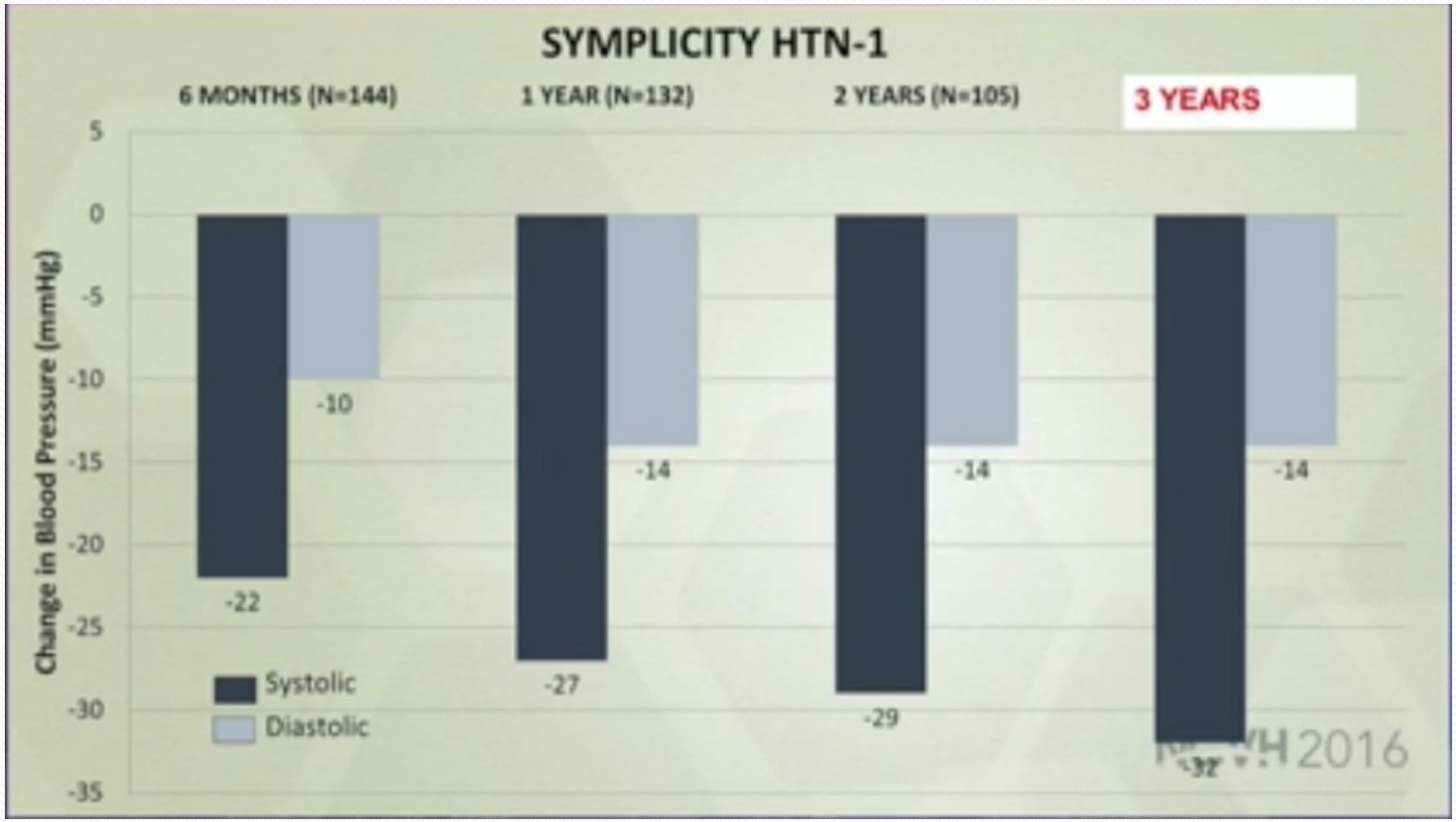
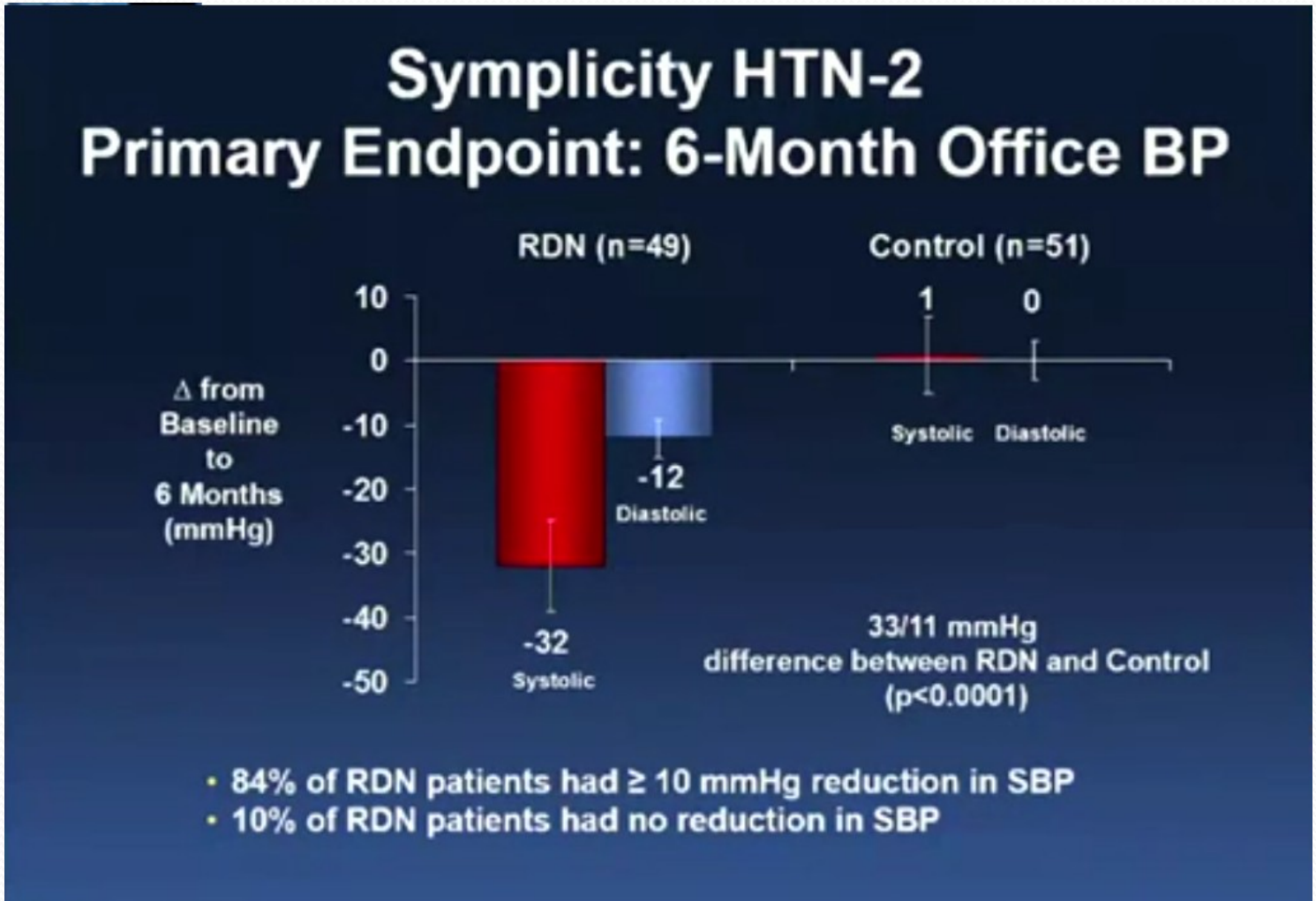


Sonuçlar mükemmel Symplicity HTN-2 planlanıyor

Symplicity HTN-2, 6aylık



European Heart Journal (2014) **35**, 1752–1759
doi:10.1093/eurheartj/ehu209

CLINICAL RESEARCH
Hypertension

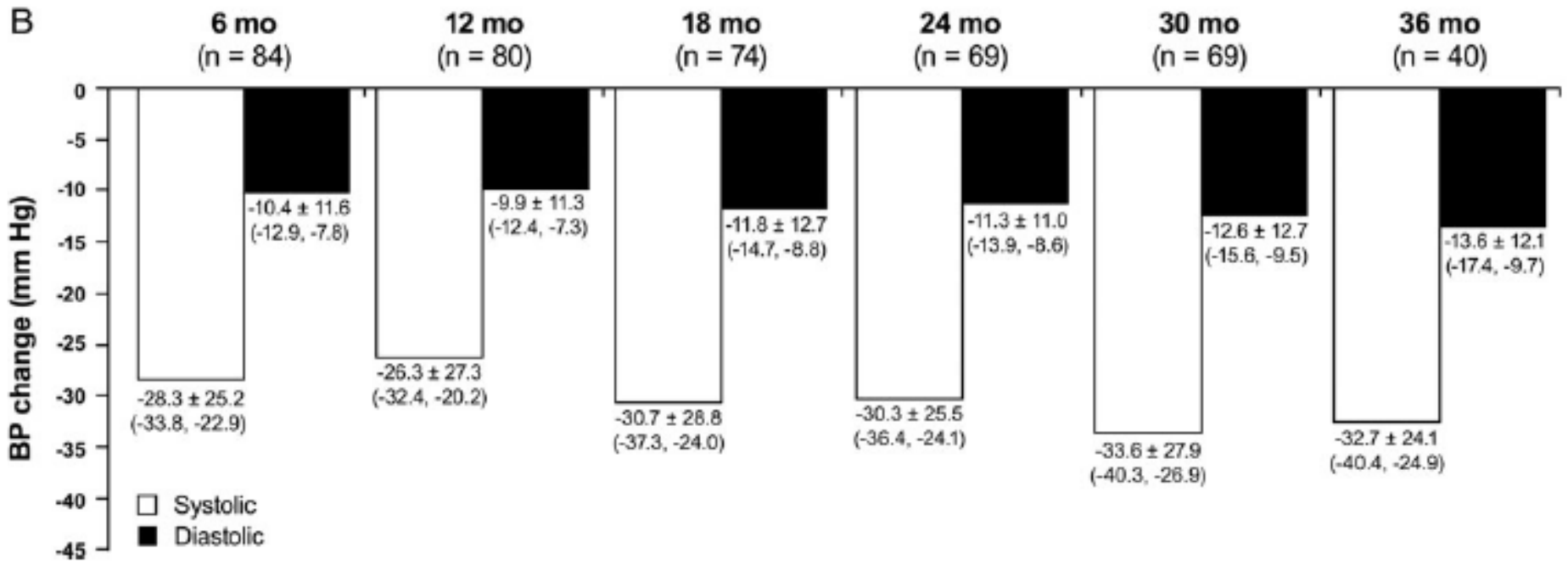
Catheter-based renal denervation for treatment of patients with treatment-resistant hypertension: 36 month results from the SYMPLICITY HTN-2 randomized clinical trial

Murray D. Esler[1]*, Michael Böhm[2], Horst Sievert[3], Christian L. Rump[4], Roland E. Schmieder[5], Henry Krum[6], Felix Mahfoud[2], and Markus P. Schlaich[1]

[1]Baker IDI Heart and Diabetes Institute, Monash University, 75 Commercial Road, Melbourne, Victoria 3004, Australia; [2]Universitätsklinium des Saarlandes, Homburg/Saar, Germany; [3]CardioVaskuläres Centrum, Frankfurt, Germany; [4]Department of Nephrology, Heinrich-Heine-University, Medical Faculty, Düsseldorf, Germany; [5]Department of Nephrology, Hypertension of the University Hospital, Clinical Research Competence Center of Hypertension and Vascular Medicine, Erlangen, Germany; and [6]Monash Centre of Cardiovascular Research and Education in Therapeutics, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

Received 3 March 2014; revised 28 April 2014; accepted 30 April 2014; online publish-ahead-of-print 4 June 2014

Symplicity HTN-2, 36aylık



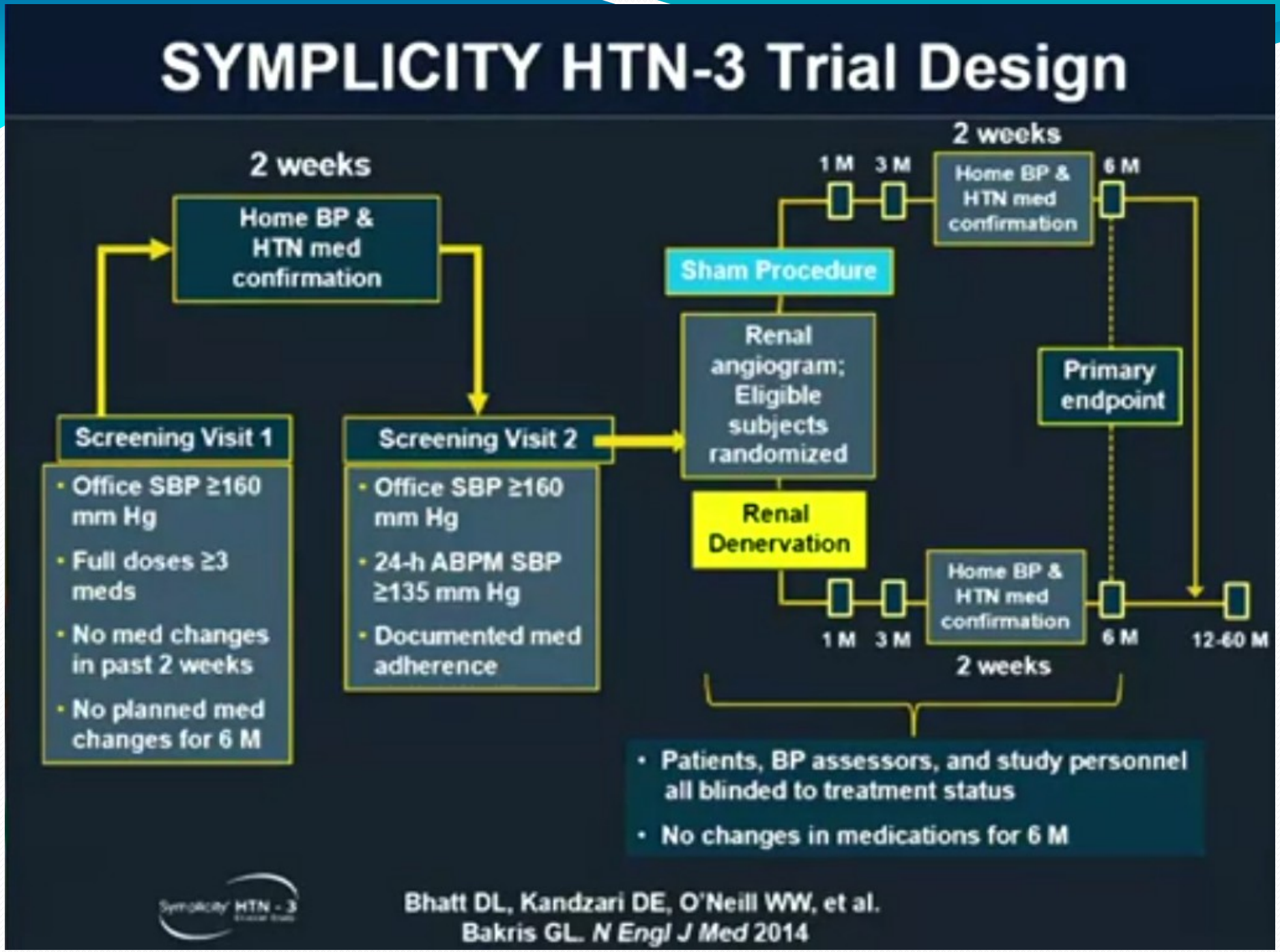
Sonuçlar mükemmel Symplicity HTN-3 planlanıyor

SYMPLICITY HTN-3

- 1441 hasta taranıp, 535 Hasta dahil edilmiş, 88 merkez, 111 operatör ,

- Hastalar 2 grup, 2:1 randomizasyon
  - Symplicity Flex Katheter (Medtronic, MN, USA) 364 hasta RSA
  - Renal angiografi (kontrol) 171 hasta.

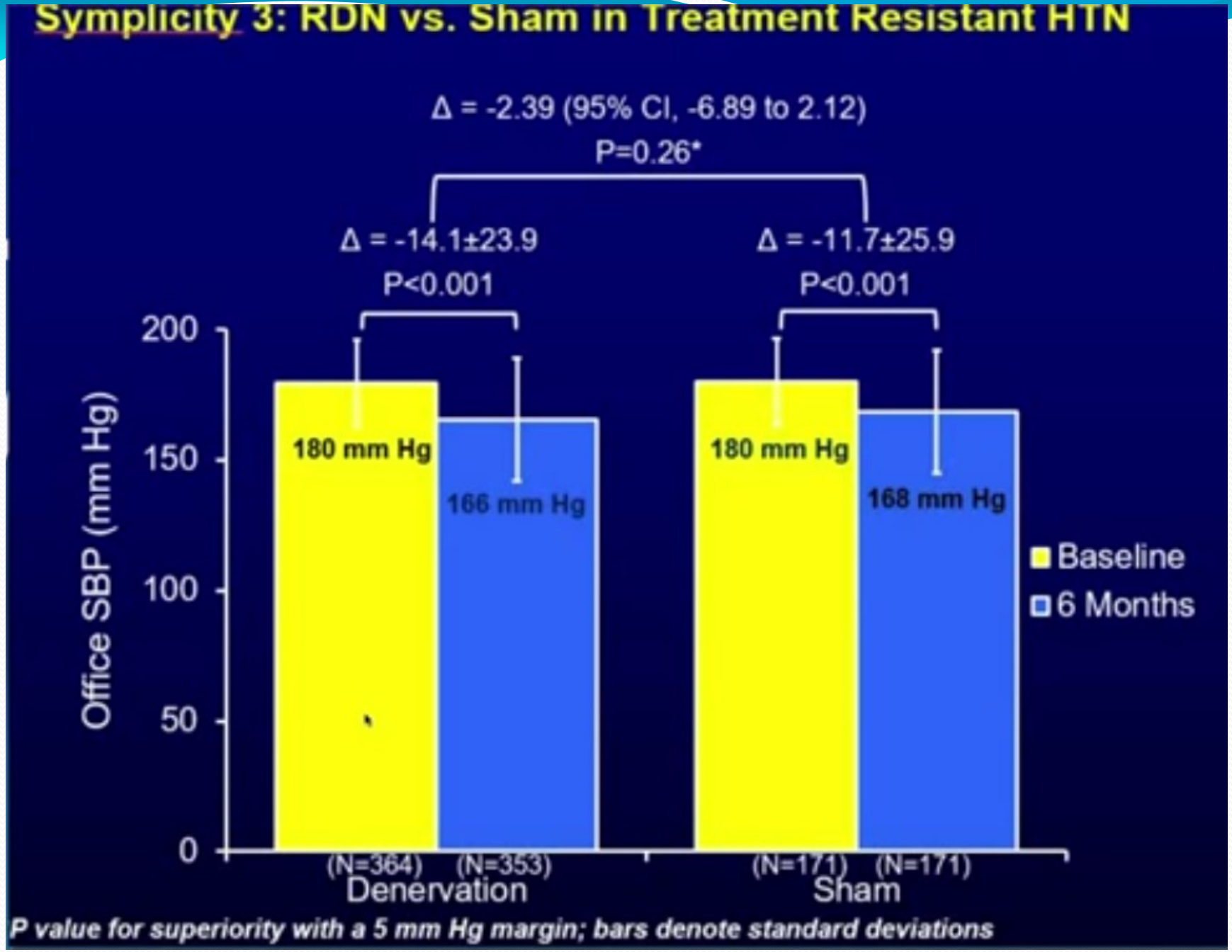
SYMPLICITY HTN-3 Trial Design

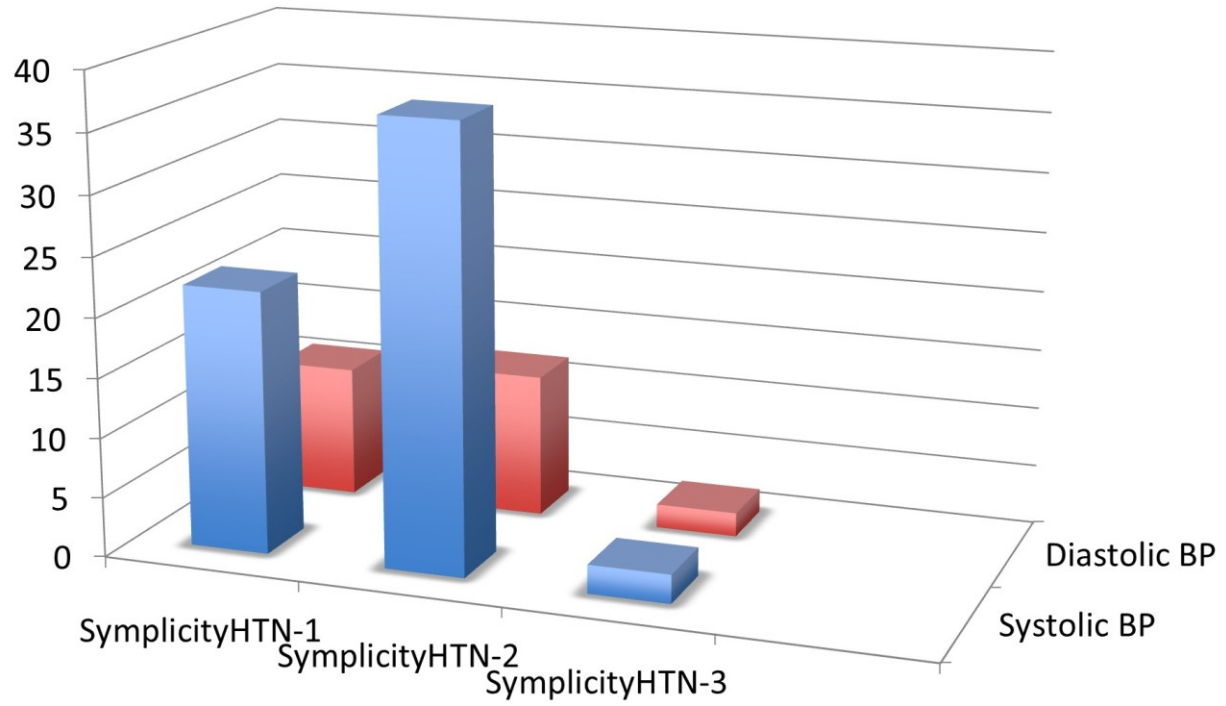


Bhatt DL, Kandzari DE, O'Neill WW, et al.
Bakris GL. *N Engl J Med* 2014

6 aylık takipte

- Primer sonlanım noktası:
  - Sistolik kan basıncında düşme
    - RSA kolunda 14.1 ± 24 mmHg
    - Kontrol kolunda 11.7 ± 26 mmHg (**P=0.255**).
- Sekonder sonlanım noktası:
  - 24-h ambulatuar BP değişim iki grupta aynı (**P=0.979**).


Symplicity 3: RDN vs. Sham in Treatment Resistant HTN
Δ = -2.39 (95% CI, -6.89 to 2.12)
P=0.26*
Δ = -14.1±23.9
P<0.001
Δ = -11.7±25.9
P<0.001
Office SBP (mm Hg)
200
150
100
50
0
180 mm Hg
166 mm Hg
180 mm Hg
168 mm Hg
Baseline
6 Months
(N=364) (N=353)
Denervation
(N=171) (N=171)
Sham
P value for superiority with a 5 mm Hg margin; bars denote standard deviations



T.F. Lüscher and F. Mahfoud. Eur. Heart J. 2014 online

Medtronic

NEWS RELEASE

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FOR IMMEDIATE RELEASE

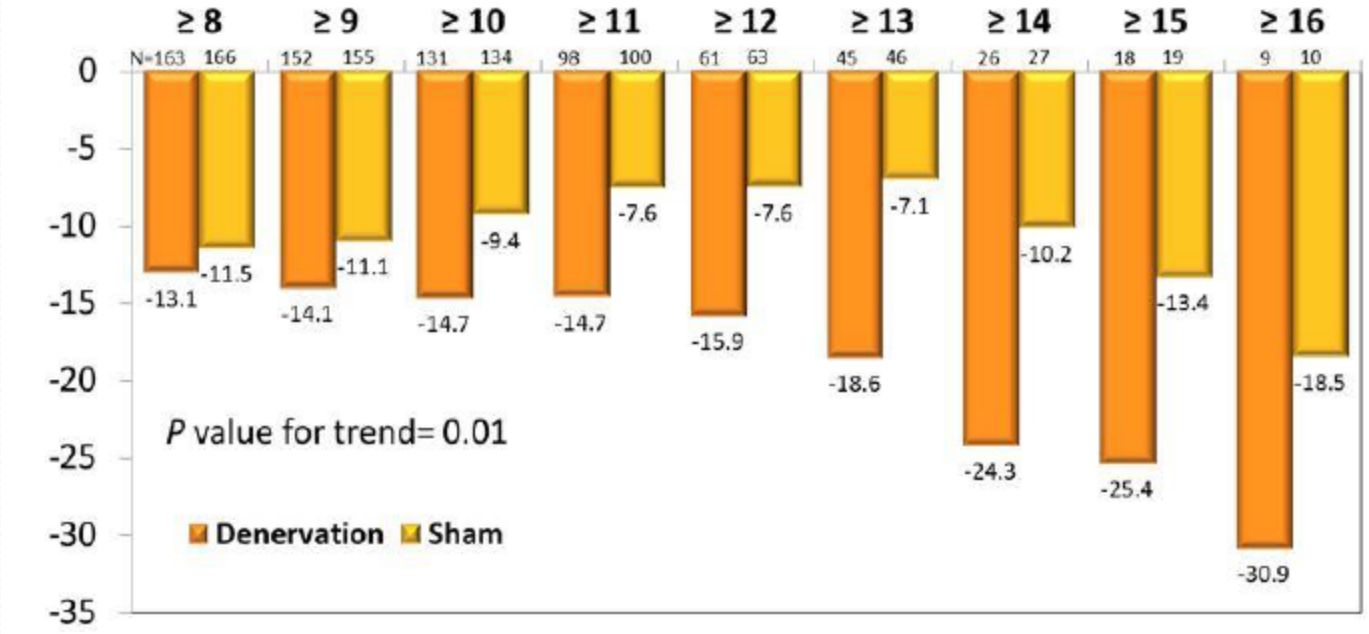
MEDTRONIC ANNOUNCES U.S. RENAL DENERVATION PIVOTAL TRIAL FAILS TO MEET PRIMARY EFFICACY ENDPOINT WHILE MEETING PRIMARY SAFETY ENDPOINT

MINNEAPOLIS – January 9, 2014 – Medtronic, Inc. (NYSE: MDT) today announced that its U.S. pivotal trial in renal denervation for treatment-resistant hypertension, SYMPLICITY HTN-3, failed to meet its primary efficacy endpoint. The trial met its primary safety endpoint, and the trial's Data Safety Monitoring Board (DSMB) concluded that there were no safety concerns in the study.

SYMPLICITY HTN-3 çalışmasının diğer çalışmalardaki başarıyı gösterememe sebepleri

- Medikal tedavi kolundaki hastalarda diğer çalışmalarda yapılmayan ilaç modifikasyonlarının yapılması (doz artımı,ilaç ayarlaması)
- 88 merkez, 111 operatör ,
- Çalışma boyunca bir operatör ortalama 3 vaka yapmış
- Öğrenme eğrisi, renal artere uygulanan ablasyon sayısı

HTN-3: More ablations cause more blood pressure reduction



	≥ 8	≥ 9	≥ 10	≥ 11	≥ 12	≥ 13	≥ 14	≥ 15	≥ 16
Baseline SBP	178.2 180.1	178.6 180.3	178.2 180.5	179.0 179.4	179.1 179.7	178.3 181.3	181.9 182.3	183.2 182.8	185.4 189.4
95% CI	-1.7(-7.1,3.7)	-3.1(-8.6,2.4)	-5.4(-11.3,0.5)	-7.1(-13.9,-0.3)	-8.4(-17.4,0.7)	-11.5(-21.8,-1.2)	-14.1(-28.8,0.7)	-12.0(-30.0,5.9)	-12.4(-44.6,19.8)
P*	0.54	0.27	0.07	0.04	0.07	0.03	0.06	0.18	0.43

Propensity scores using baseline characteristics as covariates were used to match sham control and denervation patients
*P value change in SBP for RDN compared with sham
Data presented are mean (SD)

Symplicity™

European Heart Journal (2017) **38**, 93–100
doi:10.1093/eurheartj/ehw325

CLINICAL RESEARCH
Interventional cardiology

Reduced blood pressure-lowering effect of catheter-based renal denervation in patients with isolated systolic hypertension: data from SYMPLICITY HTN-3 and the Global SYMPLICITY Registry

Felix Mahfoud[1]*, George Bakris[2], Deepak L. Bhatt[3], Murray Esler[4], Sebastian Ewen[1], Martin Fahy[5], David Kandzari[6], Kazuomi Kario[7], Giuseppe Mancia[8], Michael Weber[9], and Michael Böhm[1]

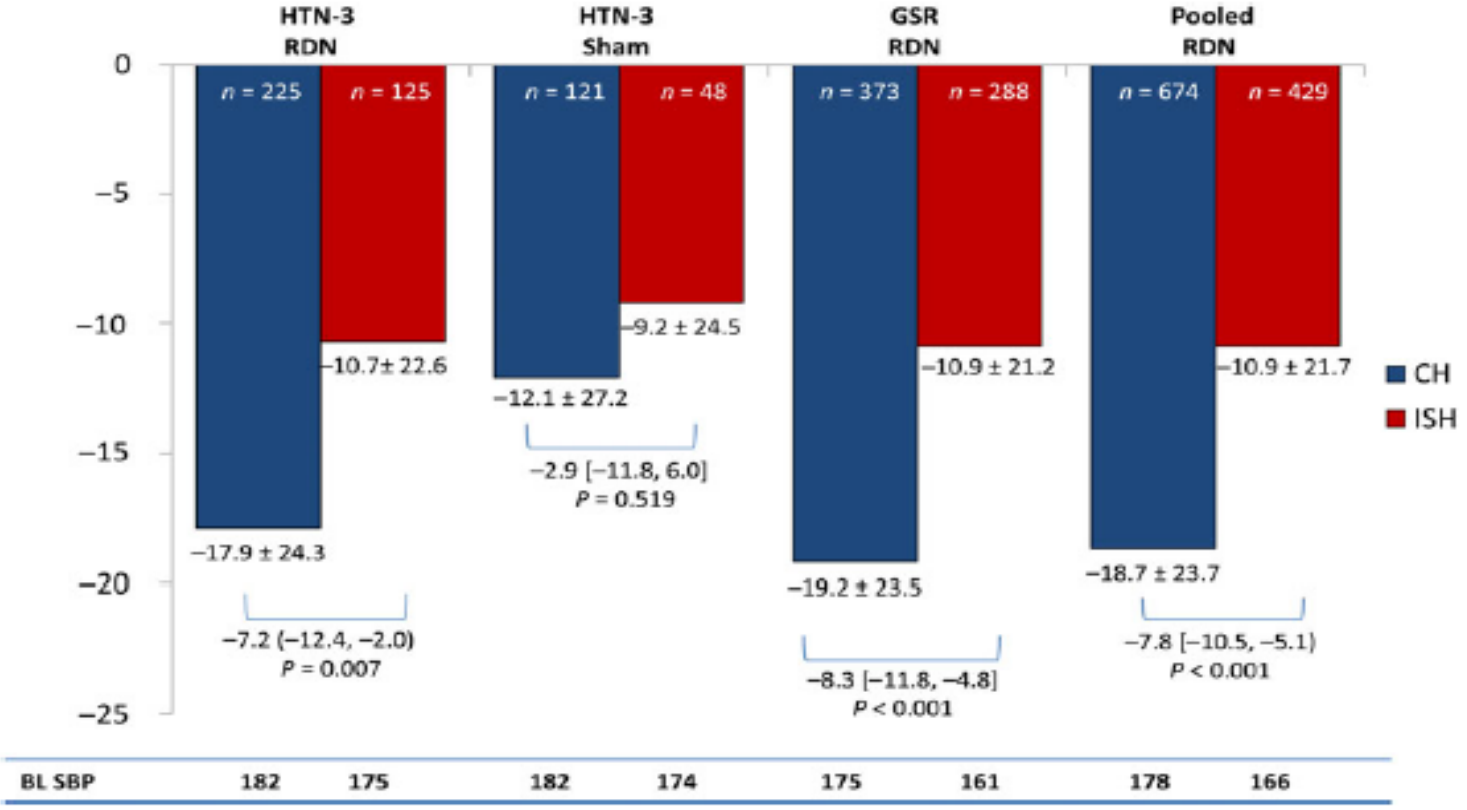
[1]Klinik für Innere Medizin III, Kardiologie, Angiologie und Internistische Intensivmedizin, Saarland University Hospital, Kirrberger Str., Geb. 40, Homburg/Saar 66421, Germany; [2]University of Chicago Medicine, Chicago, IL, USA; [3]Brigham and Women's Hospital Heart & Vascular Center and Harvard Medical School, Boston, MA, USA; [4]Baker IDI Heart and Diabetes Institute, Melbourne, Australia; [5]Medtronic, Santa Rosa, CA, USA; [6]Piedmont Heart Institute, Atlanta, GA, USA; [7]Jichi Medical University School of Medicine, Tochigi, Japan; [8]University of Milano-Bicocca and Istituto Auxologico Italiano, Milan, Italy; and [9]SUNY Downstate Medical Center, Brooklyn, NY, USA

Received 31 January 2016; revised 27 April 2016; accepted 29 June 2016; online publish-ahead-of-print 28 July 2016

See page 101 for the editorial comment on this article (doi:10.1093/eurheartj/ehw460)

Mahfoud F, EHJ 2016

- SYMPLICITY HTN-3 deki hastalar izole sistolik hipertansiyonu ve kombine hipertansiyon olan 2 gruba ayrılmış.
- 6 aylık takipte Ofis tansiyonları ölçüldüğünde
- Kombine hipertansiyonu olan bireyler RSA'dan daha fazla fayda görmüş
- Medikal tedavi koluyla karşılaştırıldığında anlamlı fark yok.



re 1 Office systolic blood pressure change at 6 months. BL, baseline; CH, combined (systolic–diastolic) hypertension; GSR, Global SYM-

- 6 aylık takipte Ambulatuar BP ölçüldüğünde
- Kombine hipertansiyonu olan bireyler RSA'dan daha fazla fayda görmüş
- Medikal tedavi koluyla karşılaştırıldığında anlamlı fark yok.

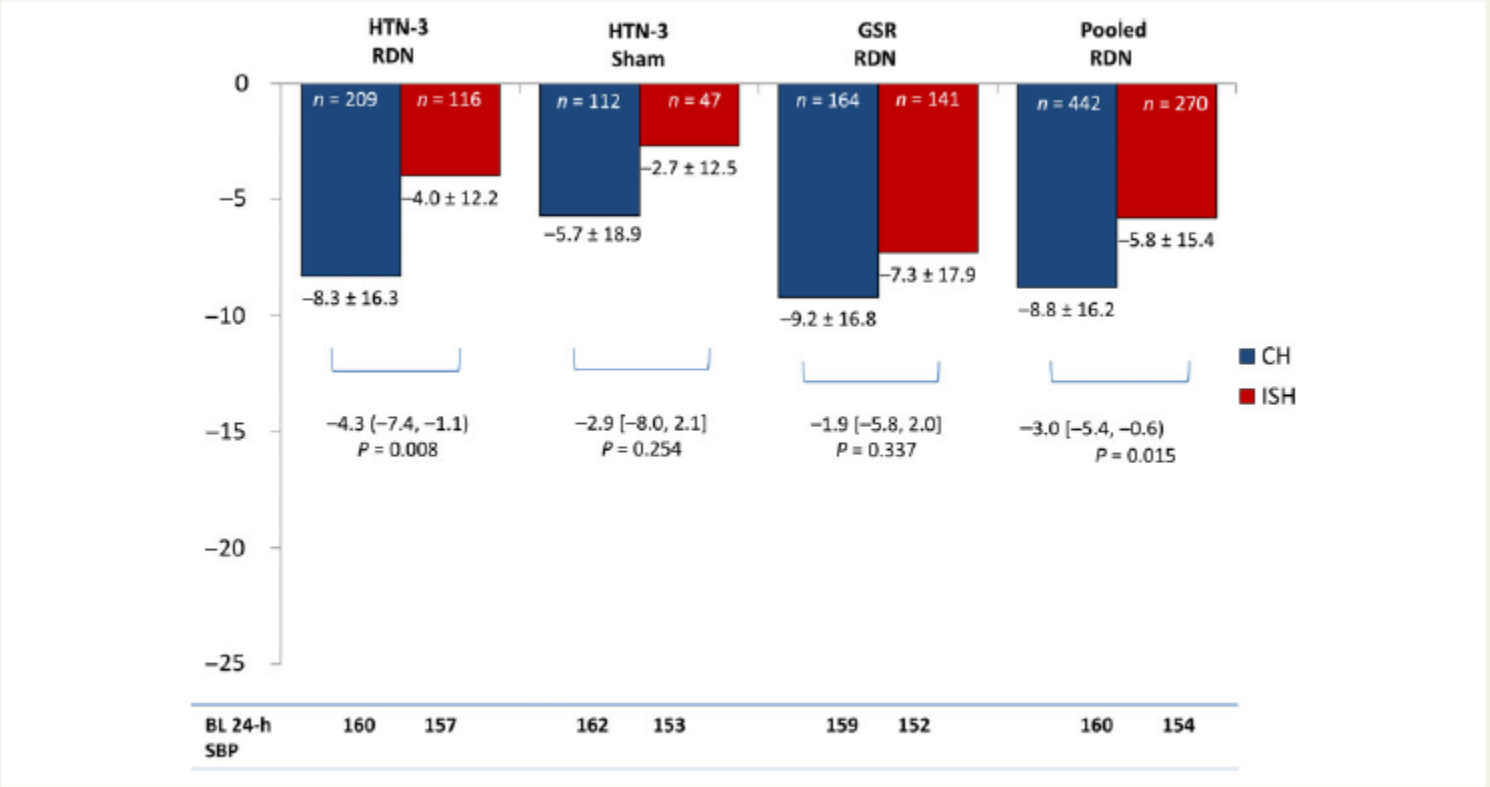


Figure 2 24-h ambulatory systolic blood pressure change at 6 months. BL, baseline; CH, combined (systolic–diastolic) hypertension; GSR, Global SYMPLICITY Registry; HTN-3, SYMPLICITY HTN-3 trial; ISH, isolated systolic hypertension; RDN, catheter-based renal denervation.

SYMPLICITY HTN-3

- Sub grup analizlerinde RSA
  - Metabolik sendrom, glukoz metabolizması üzerine
  - LVH de diastolik fonksiyon pozitif etkisi

  - Ayrıca hasta grubu
    - OSAS
    - KBY
    - KKY, Taşikardik
    - Polikistik BH hastalarında yararlı pozitif etkileri

Metabolik sendromlu HT hastalarda RSA'nun insülin rezistansı ve sempatik aktivite üzerine etkisi

Original Article

Effects of multielectrode renal denervation on elevated sympathetic nerve activity and insulin resistance in metabolic syndrome

Costas Tsioufis[a], Kyriakos Dimitriadis[a], Alexandros Kasiakogias[a], Theodore Kalos[a], Ioannis Liatakis[a], Evagelia Koutra[a], Levki Nikolopoulou[a], Athanasios Kordalis[a], Rita Omega Ella[b], Elizabeth Oi-Yan Lau[b], Guido Grassi[c,d], Vasilios Papademetriou[e], and Dimitrios Tousoulis[a]

Journal of Hypertension 2017, 35:000–000

[a]First Cardiology Clinic, National and Kapodistrian University of Athens, Hippocration Hospital, Athens, Greece, [b]St. Jude Medical, Inc., Irvine, California, USA, [c]Clinica Medica, University Milano-Biococca, [d]IRCCS Multimedica, Sesto San Giovanni, Milano, Italy and [e]Veterans Affairs and Georgetown University Medical Centers, Washington, District of Columbia, USA

Correspondence to Costas Tsioufis, MD, PhD, FESC, FACC, 114 Vas. Sofias Ave, Athens 11527, Greece. Tel: +30 213 2089522; e-mail: ktsioufis@hippocratio.gr

Received 9 September 2016 **Revised** 8 November 2016 **Accepted** 21 December 2016

J Hypertens 35:000–000

DOI:10.1097/HJH.0000000000001262

- Metabolik sendrom tanılı 17 dirençli HT hastası, 3:1 randomizasyon
  - 13 hasta RSA
  - 4 kontrol
- Ayrılıp 3 ay sonra OGTT yapılmış.
- RSA grubunda OGTT ye sekonder artmış sempatik sinir aktivitesinde azalma ($p<0,001$)
- Fakat insülin rezistansında , Tg, HDL seviyelerinde anlamlı fark yok.

RSA LVH'inde gerileme

- 66 HT hasta RSA 6 aylık takip

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ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.10.073

Hypertension

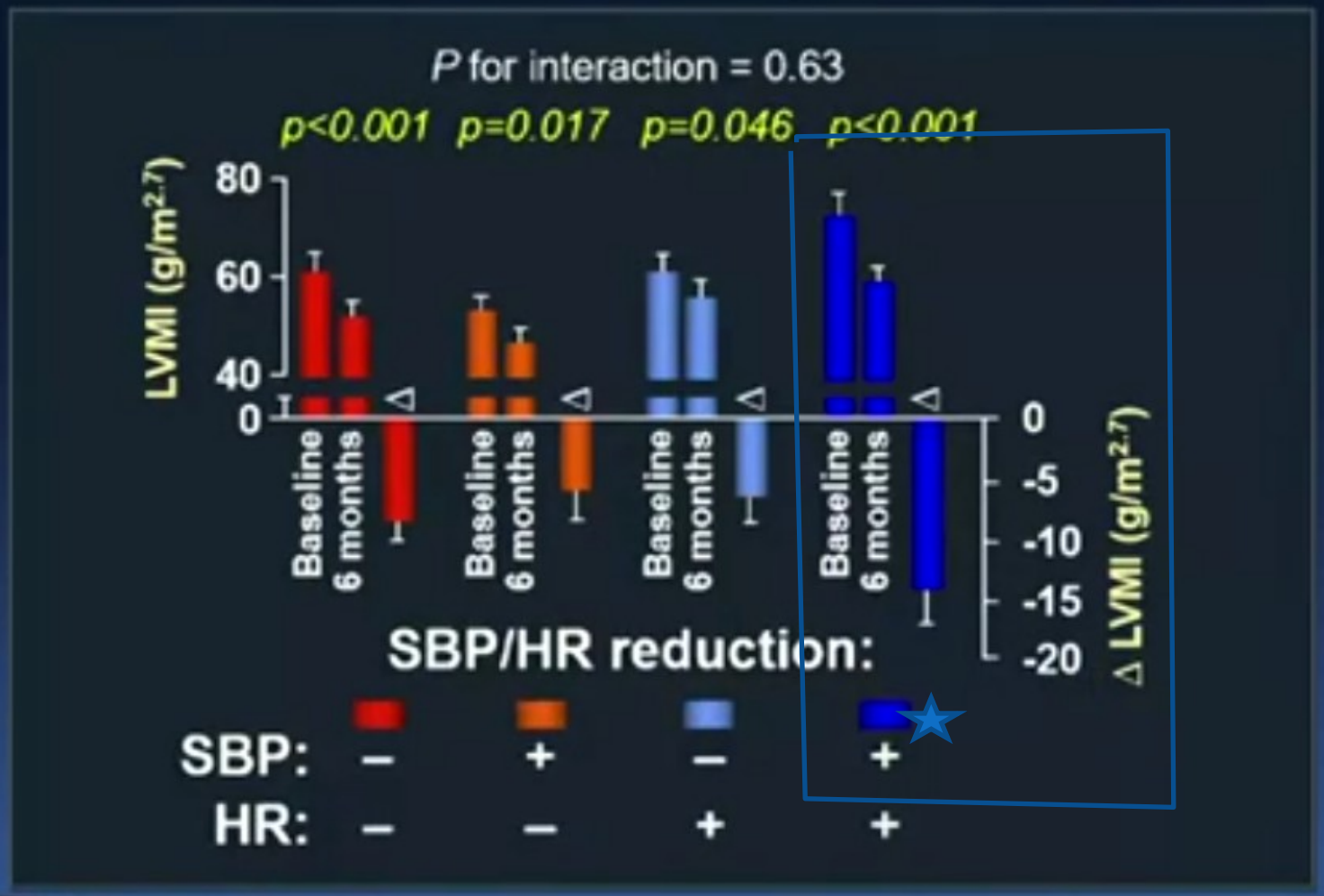
Improvements in Left Ventricular Hypertrophy and Diastolic Function Following Renal Denervation

Effects Beyond Blood Pressure and Heart Rate Reduction

Stephan H. Schirmer, MD, PhD, Marwa M. Y. A. Sayed, MD, Jan-Christian Reil, MD, Christian Ukena, MD, Dominik Linz, MD, PhD, Michael Kindermann, MD, Ulrich Laufs, MD, Felix Mahfoud, MD, Michael Böhm, MD

Homburg/Saar, Germany

Independence of LV Mass Reduction and BP or HR Reductions following RDN



Schirmer SH1, Sayed MM2, Reil JC2, Ukena C2, Linz D2, Kindermann M2, Laufs U2, Mahfoud F2, Böhm M2. Improvements in left ventricular hypertrophy and diastolic function following renal denervation: effects beyond blood pressure and heart rate reduction. J Am Coll Cardiol. 2014 May 13;63(18):1916-23. doi: 10.1016/j.jacc.2013.10.073. Epub 2013 Dec 4.

- Kalp Yetmezliği ön çalışmalar sınırlı sayıda hasta

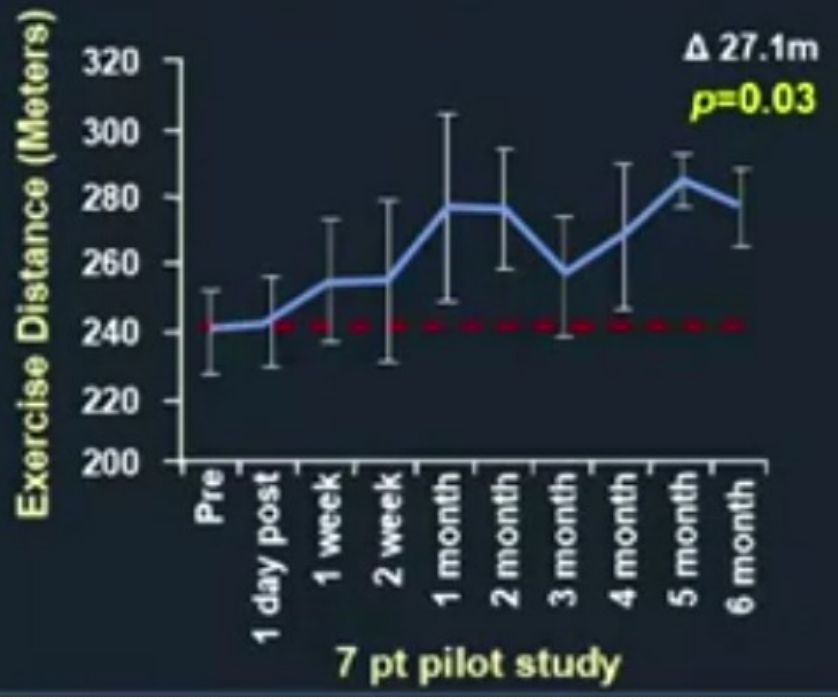
ön sunum yapılmış

- Reach – Pilot (Renal Artery Denervation in Chronic Heart Failure Study (REACH)çalışmasında RSA yapılan hastalarda 6.ayın sonunda egzersiz kapasitesi artmış (p:0,03) sadece 7 hasta . Çalışma devam ediyor (NCT 01639378)

- Olomouc -I çalışmasında 6.ayın sonunda EF de %6 lık artış (p<0,01) 21 hasta

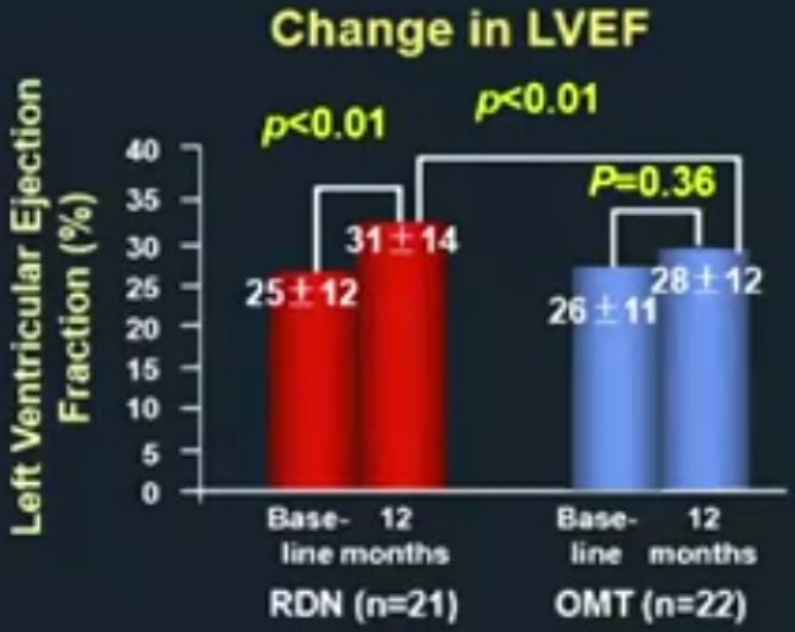
RDN for Congestive Heart Failure: Preliminary Data

REACH-Pilot: Improvement in exercise capacity



7 pt pilot study

OLOMOUC I: Improvement in ejection fraction



51 randomized pts

RSA ve KKY de 6 lık yürüme testi

Rev Port Cardiol. 2017;36(1):45–51

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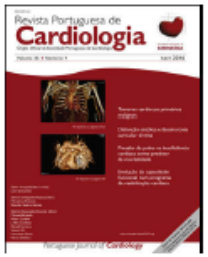
Revista Portuguesa de **Cardiologia**

Portuguese Journal of ***Cardiology***

www.revportcardiol.org



ORIGINAL ARTICLE

Effects of percutaneous renal sympathetic denervation on cardiac function and exercise tolerance in patients with chronic heart failure

Jun-Qing Gao[a], Yun Xie[b], Wei Yang[a], Jian-Pu Zheng[a], Zong-Jun Liu[a,*]

[a] *Department of Cardiology, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200062, People's Republic of China*

[b] *Department of Cardiology, People's Hospital of Shanghai Putuo District, Shanghai 200060, People's Republic of China*

Received 10 April 2016; accepted 27 July 2016

- EF<%45 olan 14 HT (ort ta:138,6±22,1 mmHg) RSA 6 ay sonra ort ta:123,2±10,5 mmHg (p:0.026)
- 6 dak lık yürüme testinde 152.9±38.0 metreden 334.3±94.4 m (p<0.001),

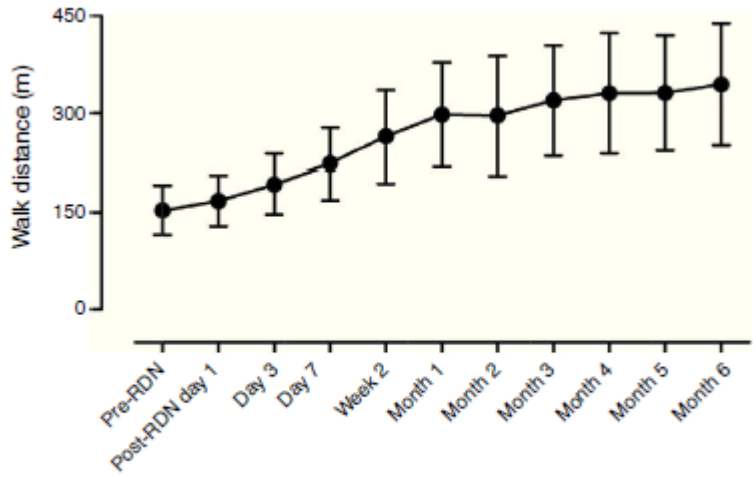


Figure 2 Six-minute walk distance in heart failure patients undergoing renal denervation. RDN: renal denervation.

OSAS ve RSA

- 10 OSAS +dirençli HT hasta ile yapılan çalışma
- RSA yapılmış 6 ay sonra apnea-hypopnea index bazale göre azalmış (median: 16.3 versus 4.5 events per hour; *P*0.059)

Hypertension

Effects of Renal Sympathetic Denervation on Blood Pressure, Sleep Apnea Course, and Glycemic Control in Patients With Resistant Hypertension and Sleep Apnea

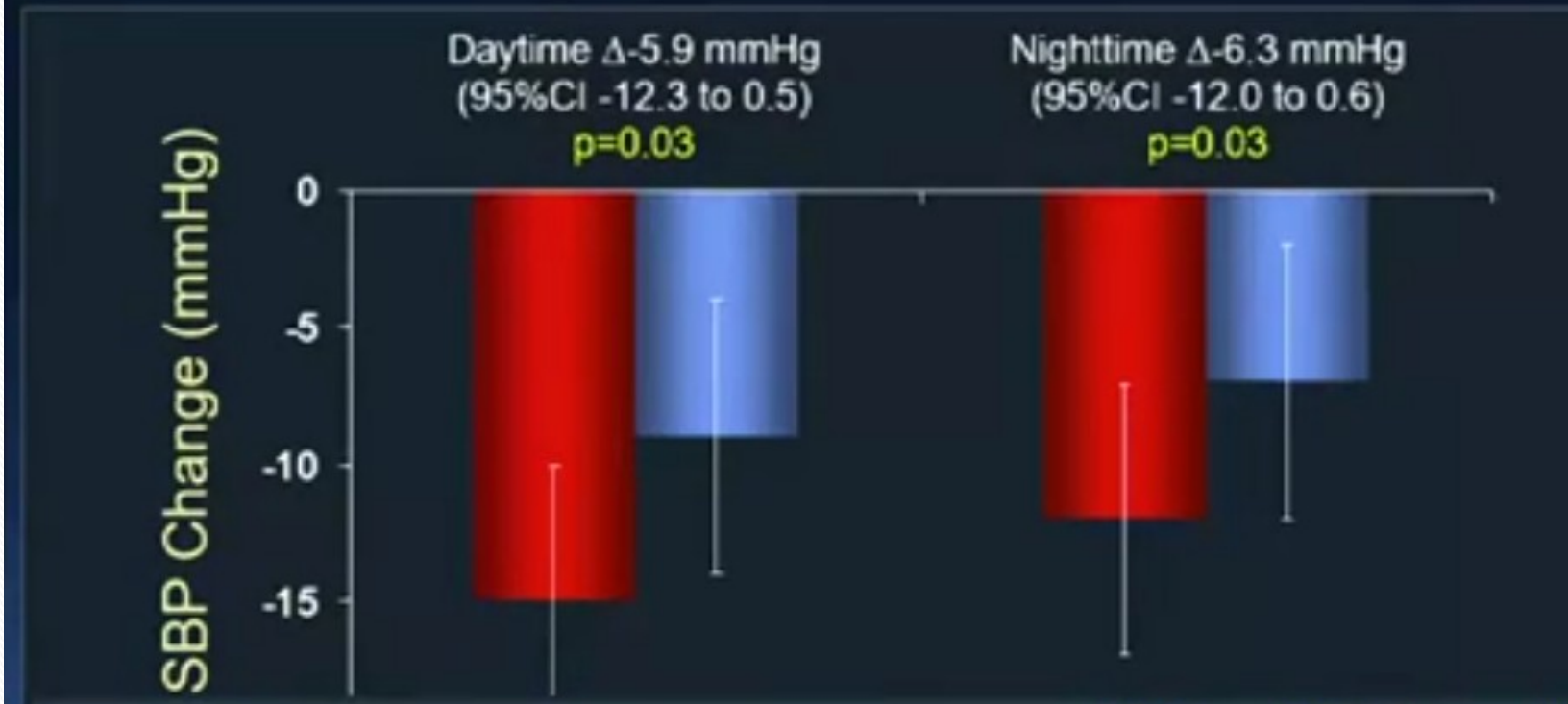
Adam Witkowski, Aleksander Prejbisz, Elżbieta Florczak, Jacek Kądziela, Paweł Śliwiński, Przemysław Bieleń, Ilona Michałowska, Marek Kabat, Ewa Warchoł, Magdalena Januszewicz, Krzysztof Narkiewicz, Virend K. Somers, Paul A. Sobotka, Andrzej Januszewicz

DOI https://doi.org/10.1161/HYPERTENSIONAHA.111.173799
Hypertension. 2011;58:559-565
Originally published September 14, 2011

DENER-HTN Çalışması

- 24 saatlik ABPM de RSA yapılan hastalarda 6.ayın sonunda gündüz saatleri veya gece saatlerinde KB düşüşünün daha iyi olduğu görülmüş
- Fakat RSA yapılmasına rağmen kullanılan ilaç dozajı azalmamış

DENER-HTN: Changes in Ambulatory BP at 6-month Follow up



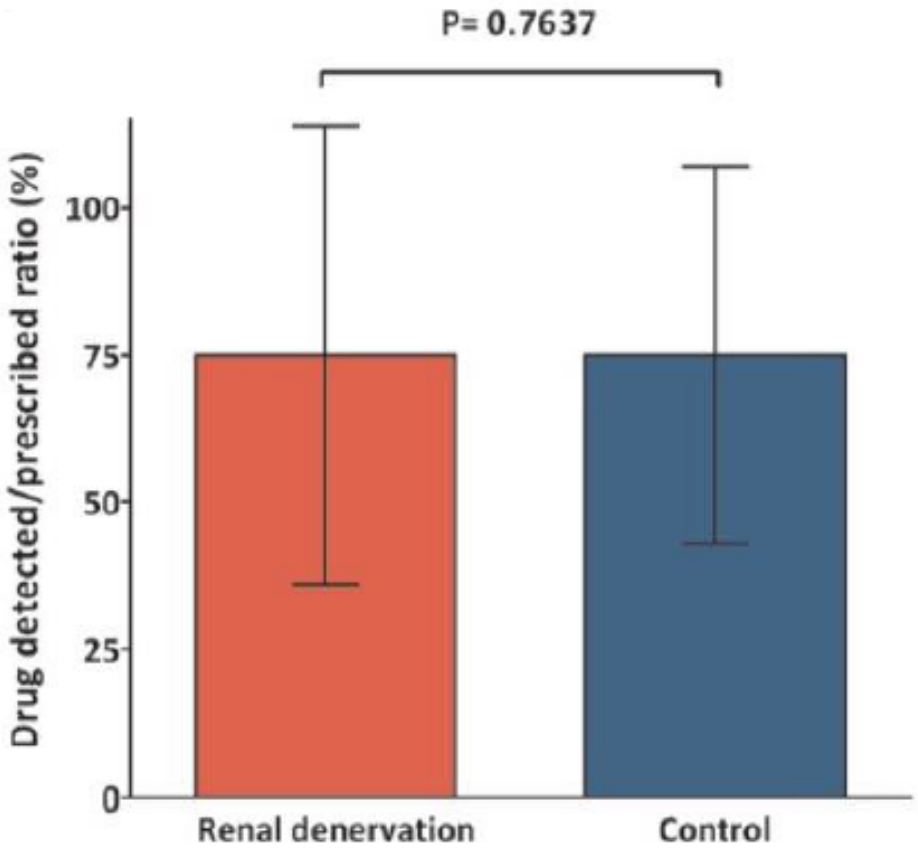
	RDN	Control	*P* value
Patients with 24-hour BP <130/80 mmHg, %	40	10	*P*=0.02
Patients with systolic BP reduction >20 mmHg, n	42	29	*P*=0.02

Denervation Control

Azizi M, Lancet 2015

- RSA grubunda kullanılan ilaç dozajı azalmamış

Adherence to Antihypertensive Treatment and the Blood Pressure–Lowering Effects of Renal Denervation in the Renal Denervation for Hypertension (DENERHTN) Trial



Azizi M, Circulation 2016

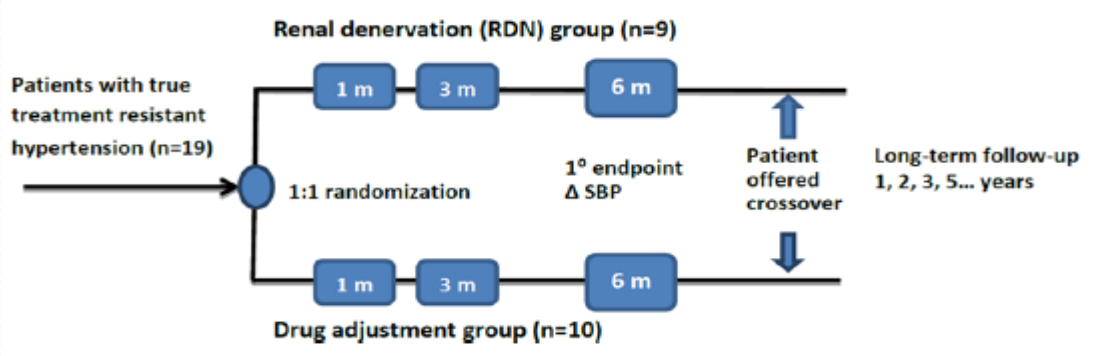
OSLO RDN çalışması

Hypertension

Adjusted Drug Treatment Is Superior to Renal Sympathetic Denervation in Patients With True Treatment-Resistant Hypertension

Fadl Elmula M. Fadl Elmula, Pavel Hoffmann, Anne C. Larstorp, Eigil Fossum, Magne Brekke, Sverre E. Kjeldsen, Eyvind Gjønnæss, Ulla Hjørnholm, Vibeke N. Kjær, Morten Rostrup, Ingrid Os, Aud Stenehjem, Aud Høieggen

DOI https://doi.org/10.1161/HYPERTENSIONAHA.114.03246
Hypertension. 2014;63:991-999
Originally published March 3, 2014



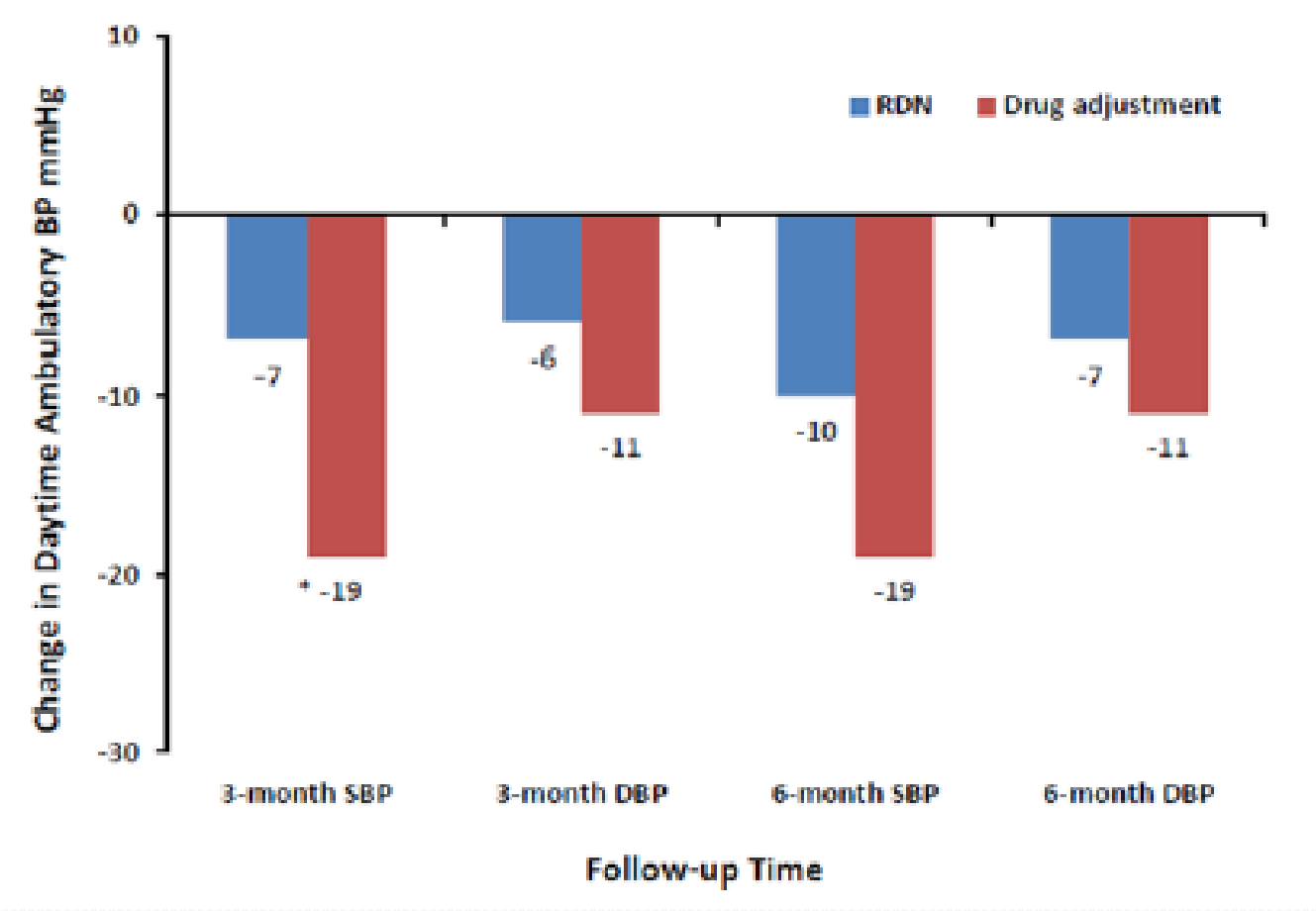
Adjusted Drug Treatment Is Superior to Renal Sympathetic Denervation in Patients With True Treatment-Resistant Hypertension (OsloRDN)

- 65 hasta dahil edilmiş fakat taramalarda dışlanarak 19 hasta
  - 10 hasta ilaç tedavisi ile kontrol
  - 9 hasta RSA yapılmış

- Çalışma 6.ay sonunda yanlız ilaç alan grup TA 160±14/88±13 mm Hg den 132±10/77±8 mm Hg (P<0.0005)
- RSA yapılmış grupta 156±13/91±15 mm Hg den 148±7/89±8 mm Hg (*P*=0.42).
- İlaç tedavisinin RSA ‘na üstün görülmesi ile etik nedenler ile çalışma 6.ayda erkenden sonlandırılmış.

Table. Baseline Characteristics, Disease History, and Antihypertensive Medication for Participants Randomized to RDN or Drug Adjustment

Variable	RDN (n=9)	Drug Adjustment (n=10)	*P* Value
No. of antihypertensive drugs	5.1 (1.6)	5.0 (1.2)	0.86
ACE inhibitors/ARBs	100% (9)	100% (10)	1.00
Calcium channel blockers	89% (8)	70% (7)	0.58
Diuretics	100% (9)	100% (10)	1.00
Aldosterone antagonist	33% (3)	60% (6)	0.37
β-Blockers	56% (5)	90% (9)	0.14
Direct renin inhibitors	22% (2)	0% (0)	0.21
α-1 blockers	56% (5)	20% (2)	0.17
Centrally acting sympathicolytics	56% (5)	40% (4)	0.66
Vasodilators	0% (0)	20% (2)	0.47


10
0
-10
-20
-30
Change in Daytime Ambulatory BP mmHg
RDN
Drug adjustment
-7
* -19
-6
-11
-10
-19
-7
-11
3-month SBP
3-month DBP
6-month SBP
6-month DBP
Follow-up Time

Role of Adding Spironolactone and Renal Denervation in True Resistant Hypertension

One-Year Outcomes of Randomized PRAGUE-15 Study

Ján Rosa, Petr Widimský, Petr Toušek, Ondřej Petrák, Karol Čurila, Petr Waldauf, František Bednář, Tomáš Zelinka, Robert Holaj, Branislav Štrauch, Zuzana Šomlóová, Miloš Táborský, Jan Václavík, Eva Kociánová, Marian Branny, Igor Nykl, Otakar Jiravský, Jiří Widimský Jr

Optimal antihypertensive treatment
(+ mineraloreceptor antagonists)

versus

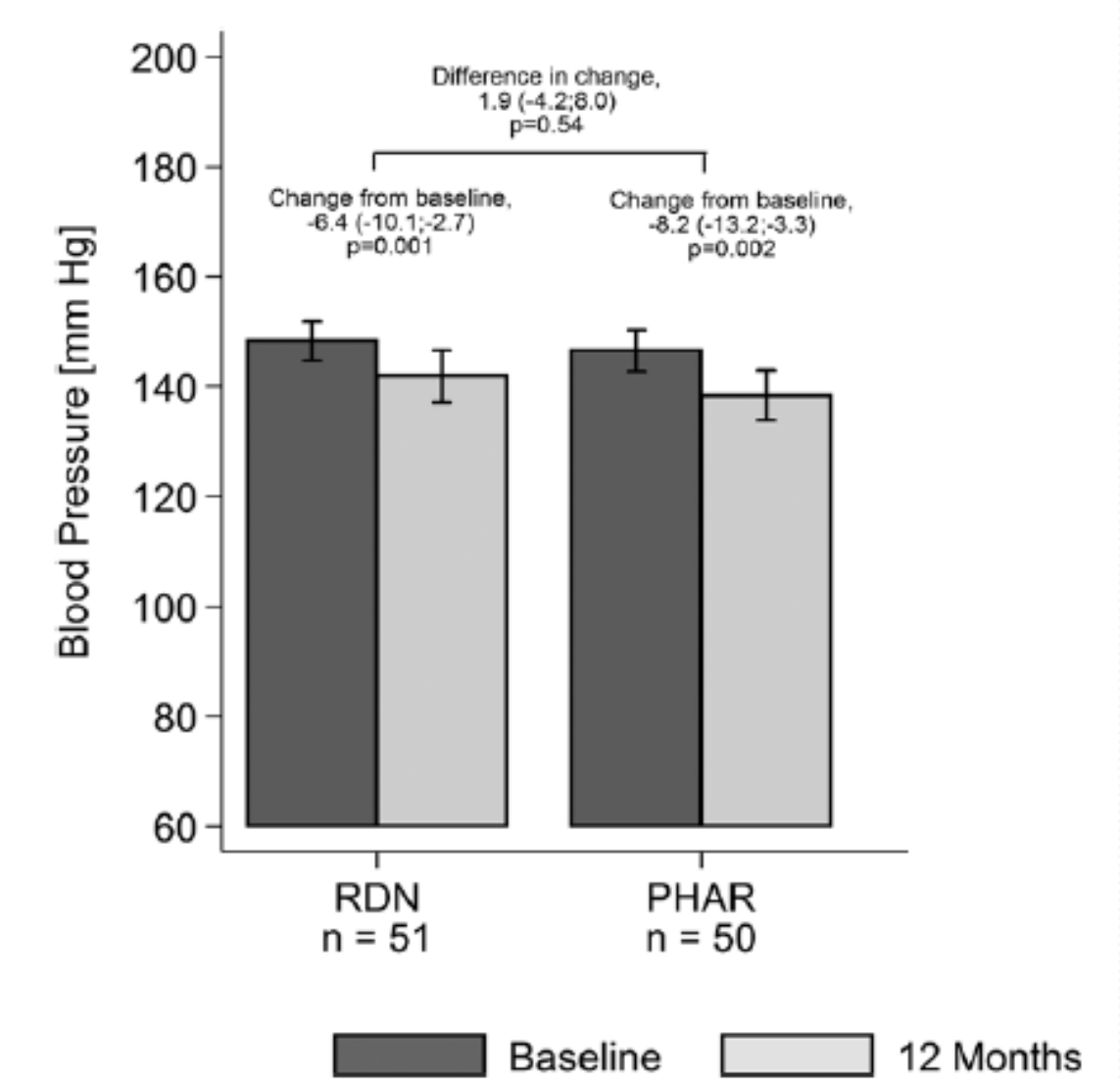
Renal denervation

Rosa J, Hypertension 2015

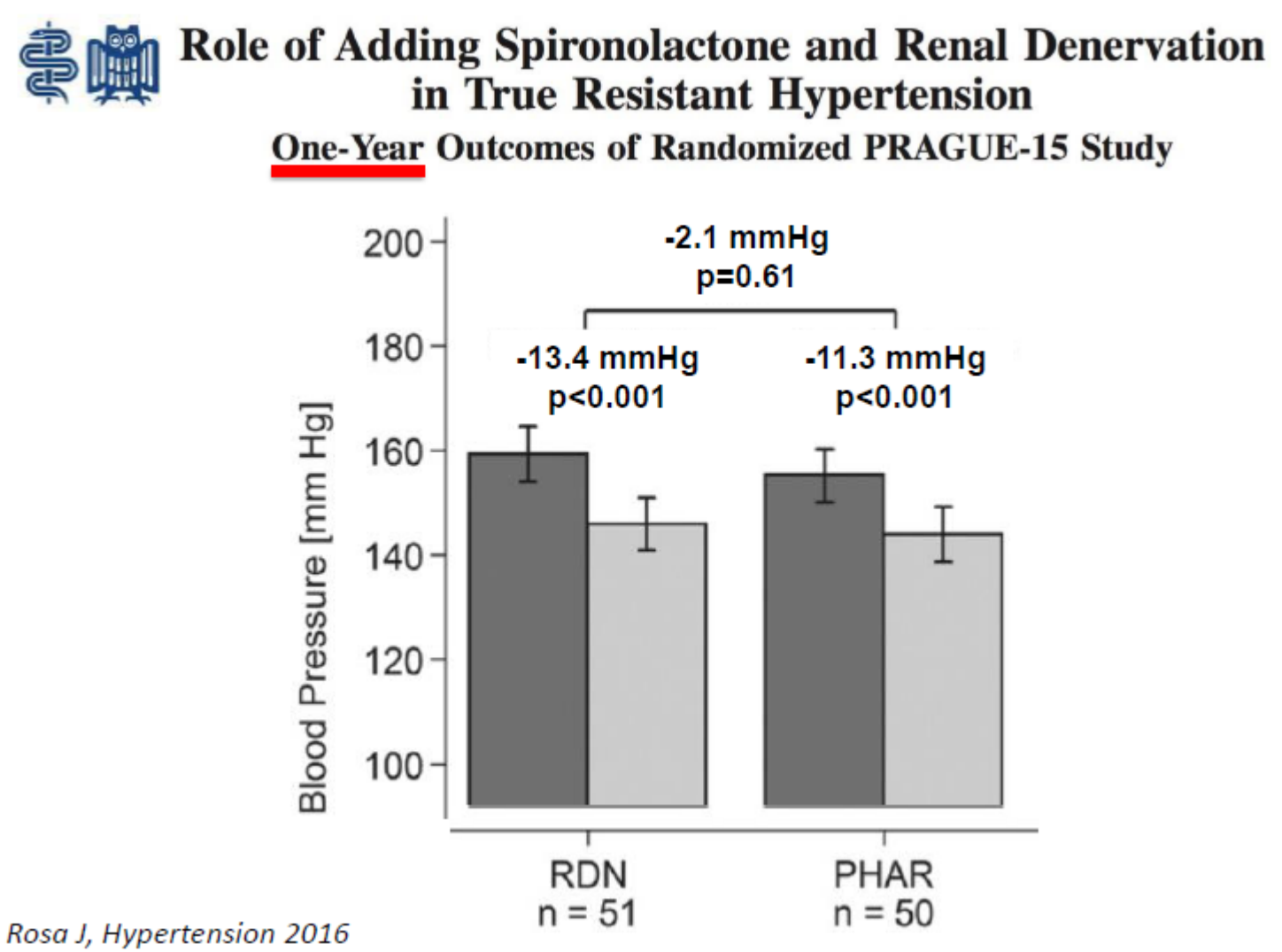
- 106 hasta
- 52 RSA+tedavi
- 54 spironalakton+tedavi

- Hastalardan 1 yıllık veri toplanmış.

24 ABPM 1.yıl sonunda



Ofis ölçümü 1.yıl sonunda



Original Article

Renal denervation in comparison with intensified pharmacotherapy in true resistant hypertension: [redacted]r outcomes of randomized PRAGUE-15 study

Ján Rosa[a,b], Petr Widimský[b], Petr Waldauf[c], Tomáš Zelinka[a], Ondřej Petrák[a], Miloš Táborský[d], Marian Branny[e], Petr Toušek[b], Karol Čurila[b], Lukáš Lambert[f], František Bednář[b], Robert Holaj[a], Branislav Štrauch[a], Jan Václavík[d], Eva Kociánová[d], Igor Nykl[e], Otakar Jiravský[e], Gabriela Rappová[e], Tomáš Indra[g], Zuzana Krátká[a], and Jiří Widimský Jr[a]

Conclusion: In the settings of true resistant hypertension, spironolactone addition (if tolerated) seems to be of better efficacy than RDN in BP reduction over a period of 24 months. However, by contrast to the 12-month results, BP changes were not significantly greater.

Received 28 September 2016
Revised 11 November 2016
Accepted 15 December 2016

PRAGUE-15 study 2.Yıl sonuç

- 106 hasta
- 52 hasta RSA+tedavi
- 54 hasta 25 mg spironalakton+tedavi

- Toplam 86 hastadan 2 yıllık veri toplanmış.

PRAGUE-15 study 2.Yıl sonuç

TABLE 2. Differences after 24 months

Variable	Change from baseline in RDN		Change from baseline in PHAR		Between-group difference in change		Between-group difference in change adjusted to baseline differences	
	mean (95% CI)	*P* Value	mean (95% CI)	*P* Value	mean (95% CI)	*P* Value	mean (95% CI)	*P* Value
Number of patients	42		44		–	–		
BMI (kg/m^2)	−0.8 (−2.1, 0.5)	0.21	0.6 (−1.2,2.5)	0.49	−1.5 (−3.7, 0.8)	0.19	−1.5 (−3.8, 0.8)	0.2
Plasma sodium (mmol/l)	−1.1 (−2.2, 0.1)	0.06	−2.0 (−3.2, −0.9)	0.001	0.9 (−0.7, 2.5)	0.26	1.1 (−0.3, 2.4)	0.12
Plasma potassium (mmol/l)	0.1 (−0.1, 0.2)	0.52	0.1 (−0.1, 0.3)	0.14	−0.1 (−0.3, 0.1)	0.41	−0.1 (−0.3, 0.1)	0.35
Creatinine [μmol/l)	0.5 (−4.1, 5.1)	0.84	3.7 (−1.9, 9.3)	0.19	−3.2 (−10.3, 3.9)	0.37	−3.0 (−10.1, 4.1)	0.4
Creatinine clearance (ml/s per 1.73 m^2)	−0.2 (−0.4, 0.1)	0.22	−0.3 (−0.6, −0.1)	0.006	0.2 (−0.2, 0.5)	0.32	0.1 (−0.2, 0.3)	0.62
Total plasma cholesterol (mmol/l)	−0.1 (−0.4, 0.1)	0.26	−0.4 (−0.7, −0.1)	0.004	0.3 (−0.1, 0.5)	0.17	0.1 (−0.2, 0.4)	0.42
Fasting plasma glucose (mmol/l)	−0.4 (−1.0, 0.1)	0.08	0.2 (−0.4, 0.8)	0.57	−0.6 (−1.4, 0.2)	0.11	−0.6 (−1.2, 0.1)	0.08
Office SBP (mmHg)	−17.7 (−24.7, −10.8)	<0.001	−14.1 (−20.1, −8.0)	<0.001	−3.6 (−12.7, 5.5)	0.43	−0.5 (−7.5, 6.7)	0.89
Office DBP (mmHg)	−12.6 (−16.6, −8.5)	<0.001	−8.3 (−12.4, −4.2)	<0.001	−4.3 (−9.9, 1.4)	0.14	−2.6 (−7.2, 2.1)	0.27
HR (bpm)	−4.5 (−8.4,− 0.5)	0.02	−5.7 (−9.6, −1.8)	0.005	1.2 (−4.2, 6.7)	0.66	1.0 (−3.8, 5.8)	0.69
24 h SBP (mmHg)	−9.1 (−13.3, −4.9)	0.001	−10.9 (−16.4, −5.5)	0.001	1.8 (−5.0, 8.6)	0.59	2.9 (−3.1, 8.8)	0.34
24 h DBP (mmHg)	−5.7 (−7.7, −3.6)	<0.001	−7.4 (−10.3, −4.5)	<0.001	1.7 (−1.8, 5.2)	0.34	2.2 (−1.0, 5.4)	0.17
24 h HR (bpm)	−0.8 (−3.2, 1.6)	0.49	−1.6 (−3.7, 0.6)	0.15	0.8 (−2.4, 3.9)	0.64	0.6 (−2.4, 3.7)	0.68
Number of drugs used	0.3 (−0.1, 0.6)	0.1	0.1 (−0.1, 0.4)	0.28	0.1 (−0.3, 0.5)	0.53	0.1 (−0.3, 0.5)	0.7

CI, confidence interval; HR, heart rate; PHAR, pharmacological treatment arm; RDN, renal denervation arm.

PRAGUE-15 study 2.Yıl sonuç

- Benzer ofis ölçümlerinde sist.TA de düşme p:0.89
  - Standart tedavi+ RSA 17,7 mmHg düşme
  - Standart tedavi +Spironolakton 14,1 mmHg düşme

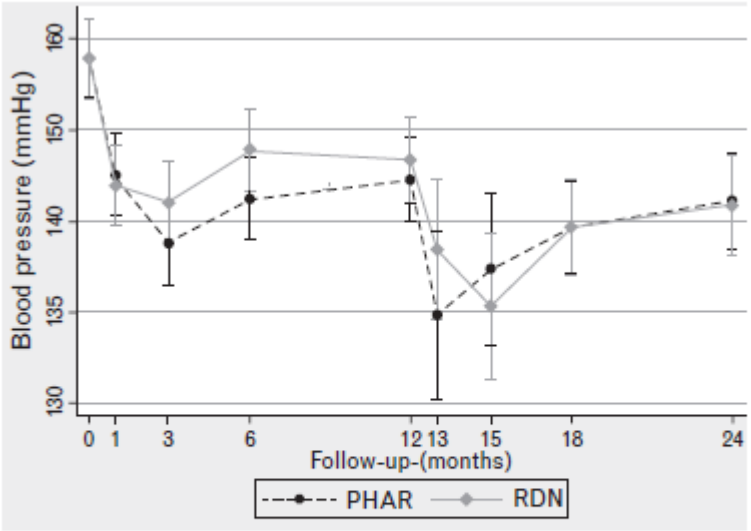


FIGURE 3 Changes of office SBP. Significant office SBP changes from baseline to 24 months were observed. The figure shows the model of office SBP during the follow-up, using the linear multilevel effect model. The data are adjusted to baseline differences and showed with 95% confidence interval. PHAR, pharmacological treatment arm; RDN, renal denervation arm.

PRAGUE-15 study 2.Yıl sonuç

- Benzer 24 sa ABPM sist TA de düşme, p:0.34
  - Standart tedavi+ RSA 9,1 mmHg düşme
  - Standart tedavi +Spironolakton 10,9 mmHg düşme

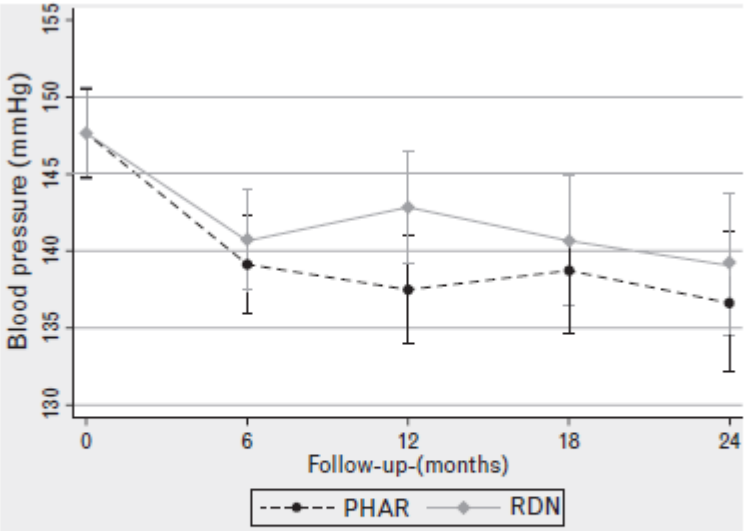


FIGURE 2 Changes of 24-h SBP. Significant 24-h SBP changes from baseline to 24 months were observed. The figure shows the model of 24-h SBP during the follow-up, using the linear multilevel effect model. The data are adjusted to baseline differences and showed with 95% confidence interval. PHAR, pharmacological treatment arm; RDN, renal denervation arm.

PRAGUE-15 study 2.Yıl sonuç

- Sonuç:
- Tedaviye dirençli hipertansiyonlu hastalarda tolere edilebiliyor ise spironolakton eklemek RSA dan daha etkili görünmekte

Spironolakton

ORIGINAL ARTICLE

Renal Denervation vs. Spironolactone in Resistant Hypertension: Effects on Circadian Patterns and Blood Pressure Variability

Alejandro de la Sierra,[1] Julia Pareja,[2] Pedro Armario,[3] Ángela Barrera,[1] Sergi Yun,[1] Susana Vázquez,[4] Laia Sans,[4] Julio Pascual,[4] and Anna Oliveras[4]

BACKGROUND
Sympathetic renal denervation (SRD) has been proposed as a therapeutic alternative for patients with resistant hypertension not controlled on pharmacological therapy. Two studies have suggested an effect of SRD in reducing short-term blood pressure variability (BPV). However, this has not been addressed in a randomized comparative trial. We aimed to compare the effects of spironolactone and SRD on circadian BP and BPV.

METHODS
This is a *post-hoc* analysis of a randomized trial in 24 true resistant hypertensive patients (15 men, 9 women; mean age 64 years) comparing 50 mg of spironolactone (n = 13) vs. SRD (n = 11) on 24-hour BP. We report here the comparative effects on daytime (8 AM–10 PM) and nighttime (0 AM–6 AM) BP, night-to-day ratios and BP and heart rate variabilities (SD and coefficient of variation of 24-hour, day and night, as well as weighted SD and average real variability (ARV)).

RESULTS
Spironolactone was more effective than SRD in reducing daytime systolic (P = 0.006), daytime diastolic (P = 0.006), and nighttime systolic (P = 0.050) BP. No differences were observed in the night-to-day ratios. In contrast, SRD-reduced diastolic BPV (24 hours, daytime, nighttime, weighted, and ARV; all P < 0.05) with respect to spironolactone, without significant differences in systolic BPV.

CONCLUSION
Spironolactone is more effective than SRD in reducing ambulatory BP. However, BPV is significantly more reduced with SRD. This effect could be important in terms of potential prevention beyond BP reduction and deserves further investigation.

Keywords: blood pressure; blood pressure variability; circadian blood pressure profile; hypertension; resistant hypertension; spironolactone; sympathetic renal denervation.

doi:10.1093/ajh/hpw085

American Journal of Hypertension 30(1) January 2017

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Keywords: blood pressure; blood pressure variability; circadian blood pressure profile; hypertension; resistant hypertension; spironolactone; sympathetic renal denervation.

doi:10.1093/ajh/hpw085

- 24 dirençli HT 1:1 randomizasyon
  - Standart tedavi+ RSA: 11 hasta
  - Standart tedavi + 50 mg Spironolakton:
- Sonuç: 6.ayın sonunda Standart tedavi + 50 mg Spironolakton eklemek daha fazla KB düşüşü sağlamış p:0,006

Table 2. Diurnal and nocturnal blood pressures and heart rate, as well as night-to-day ratios according to treatment group

Parameter	Spironolactone			Renal denervation			*P* value*
	Baseline	6 months	Difference	Baseline	6 months	Difference	
Daytime [illegible], mm Hg	158.1±9.9	132.6±17.1	[illegible]±17.0	153.0±8.3	149.5±9.5	[illegible]±12.8	[illegible]
Daytime DBP, mm Hg	83.0±10.0	72.8±9.2	−10.3±8.4	84.2±10.3	82.4±8.8	−1.8±8.3	0.006
Daytime HR, bpm	70.3±10.3	72.6±9.1	2.3±7.9	66.4±7.7	68.8±8.7	2.4±7.6	0.631
Nighttime SBP, mm Hg	146.5±15.6	123.2±14.7	−23.4±15.6	141.2±11.4	134.1±22.2	−7.1±18.2	0.050
Nighttime DBP, mm Hg	75.1±12.4	64.0±9.2	−11.1±9.7	75.4±8.6	71.5±13.6	−3.9±9.6	0.066
Nighttime HR, bpm	62.7±9.9	62.7±10.4	0.1±7.7	56.5±6.9	58.9±8.4	2.5±6.8	0.775
NDR SBP, %	92.7±7.7	93.2±6.2	0.6±8.0	92.5±9.3	89.7±13.3	−2.8±8.4	0.313
NDR DBP, %	90.3±8.8	88.1±8.2	−2.2±7.9	90.1±8.9	86.7±12.6	−3.4±8.6	0.711
NDR HR, %	89.6±9.1	86.5±11.0	−3.1±12.2	85.6±10.9	86.0±8.8	0.4±13.9	0.976

Randomize Çalışmaların Metaanalizi

Blood Pressure

Taylor & Francis
Taylor & Francis Group

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Meta-analysis of randomized controlled trials of renal denervation in treatment-resistant hypertension

Fadl Elmula M. Fadl Elmula, Yu Jin, Wen-Yi Yang, Lutgarde Thijs, Yi-Chao Lu, Anne C. Larstorp, Alexandre Persu, Marc Sapoval, Ján Rosa, Petr Widimský, Lotte Jacobs, Jean Renkin, Ondřej Petrák, Gilles Chatellier, Kazuyuki Shimada, Jiři Widimský, Kazuomi Kario, Michel Azizi, Sverre E. Kjeldsen, Jan A. Staessen & For The European Network Coordinating Research On Renal Denervation (ENCOReD) Consortium

- 24 sa systolic BP 6.ayın sonunda 95% CI ile karşılaştırıldığında (p:0.11).
- RSA farmakolojik tedaviye üstünlük sağlayamamıştır

	Control		RDN	
	N°	Δ (SD)	N°	Δ (SD)
SYMPLICITY-2	25	−3 (19)	20	−11 (15)
SYMPLICITY-3	162	−4.8 (17)	329	−6.8 (15)
OSLO	10	−21 (13)	9	−10 (11)
PRAGUE	54	−8.1 (17)	52	−8.6 (12)
DENER	53	−9.5 (13)	48	−15.4 (13)
SYMPLICITY-F	35	−3.5 (10)	32	−7.0 (11)
SYMPLICITY-J	19	−1.4 (10.2)	22	−7.5 (12)
ALL	358	−6.7 (−11.2, -2.2)	512	−9.2 (−12.2, −6.2)
		P=0.011		*P*<0.001

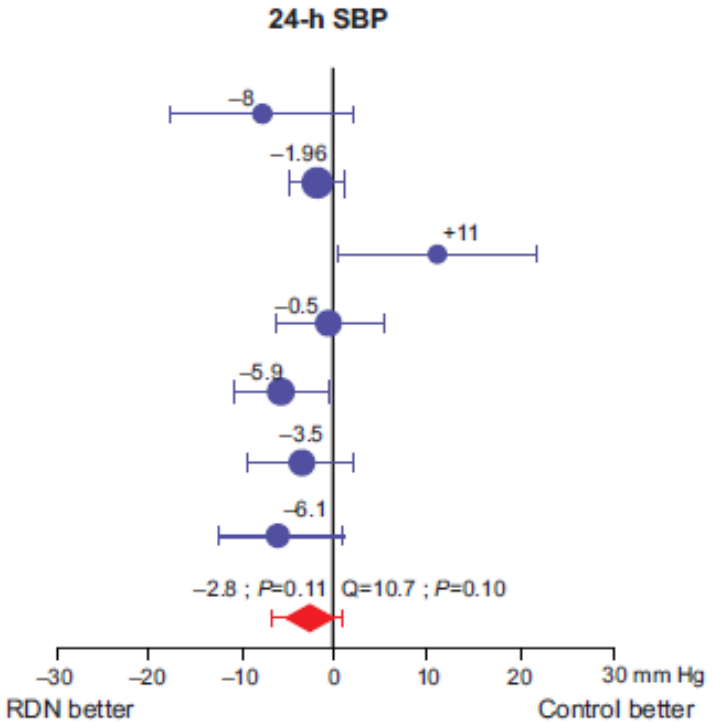
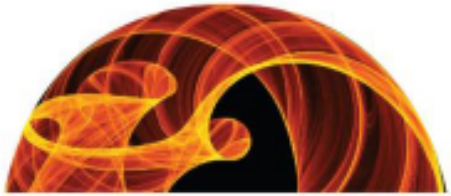


Figure 3. Six-month response of 24 h systolic blood pressure (SBP) to renal denervation (RDN) or to follow-up in the control group. Solid points represent the effect size in individual studies and have a size proportional to the inverse of the variance. The diamond represents the pooled estimate. Horizontal lines and diamonds denote the 95% confidence intervals (CIs). For all trials combined, the pooled within-group change is given with 95% CI. P-values refer to the significance of the pooled between-group estimate and Cochran's *Q* test for heterogeneity.

SPYRAL HTN

Global Clinical Trial Program

OFF – n=100
ON – n=100



THE RADIANCE-HTN STUDY

A Study of the ReCor Medical Paradise® System in Clinical Hypertension

SOLO – n=146
ON – n=146

REDUCE-HTN: REINFORCE Study OFF – n=100

ABLATIVE SOLUTIONS

Target BP I OFF – n=100

ENLIGHTNED

GLOBAL IDE TRIAL

FIX – n=???

Spyral HTN Global Clinical Trial Program

First Phase

SPYRAL HTN–OFF MED

- Up to 100 patients
- Sham RCT (1:1)
- Main body and branch ablation
- No specific baseline medication requirement
- Compare ABPM change at 3 months

SPYRAL HTN–ON MED

- Up to 100 patients
- Sham RCT (1:1), 3 medication classes
- Main body and branch ablation
- No max tolerated dose
- Compare ABPM change at 3 months

Second Phase

SPYRAL HTN Pivotal

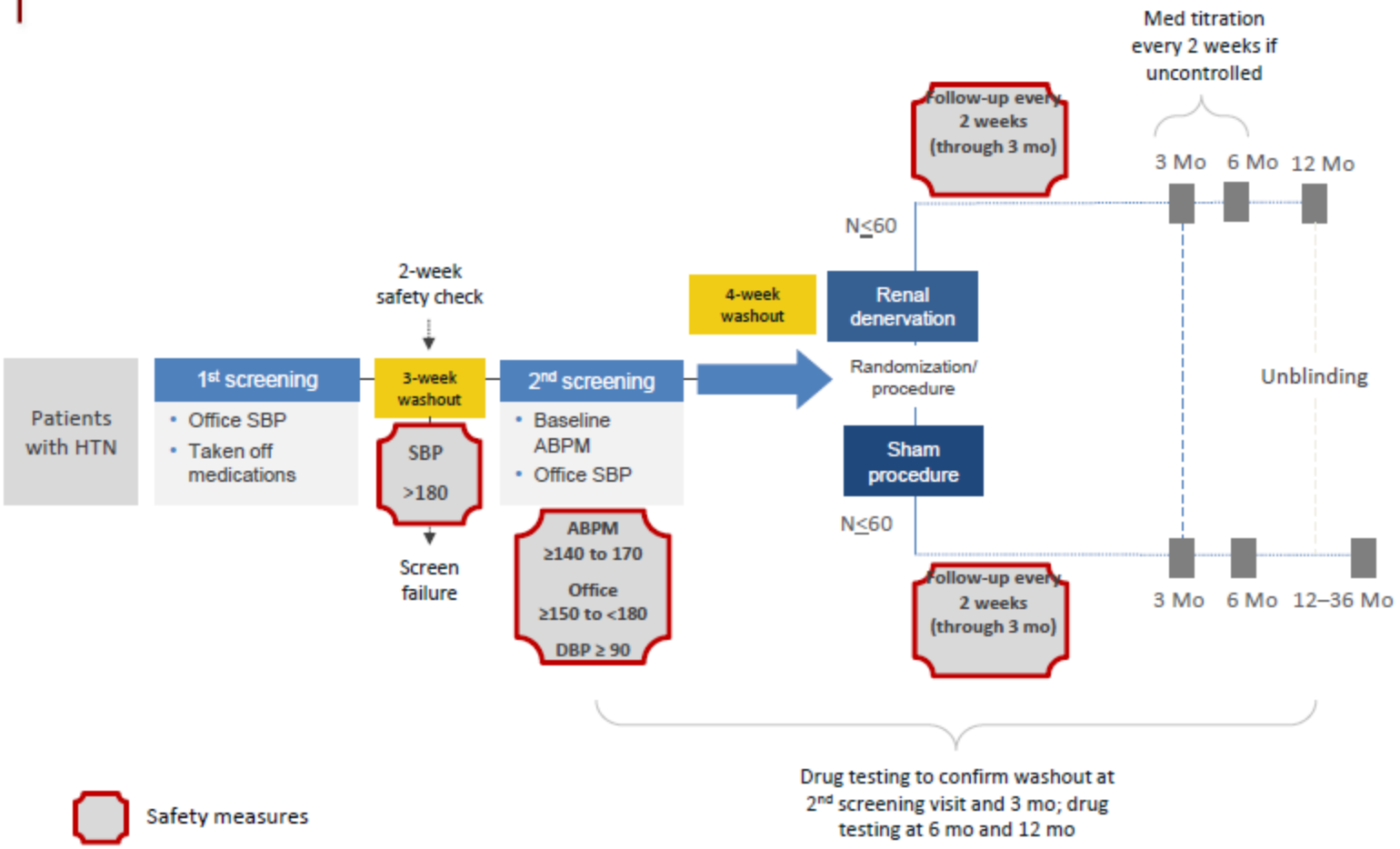
- Based on OFF/ON trial results
- Cost effectiveness data/QOL to be measured

TRIAL REGISTRATION:
ClinicalTrials.gov NCT02439749 NCT02439775.

Kandzari et al. Am Heart J 2015

Piedmont HEART

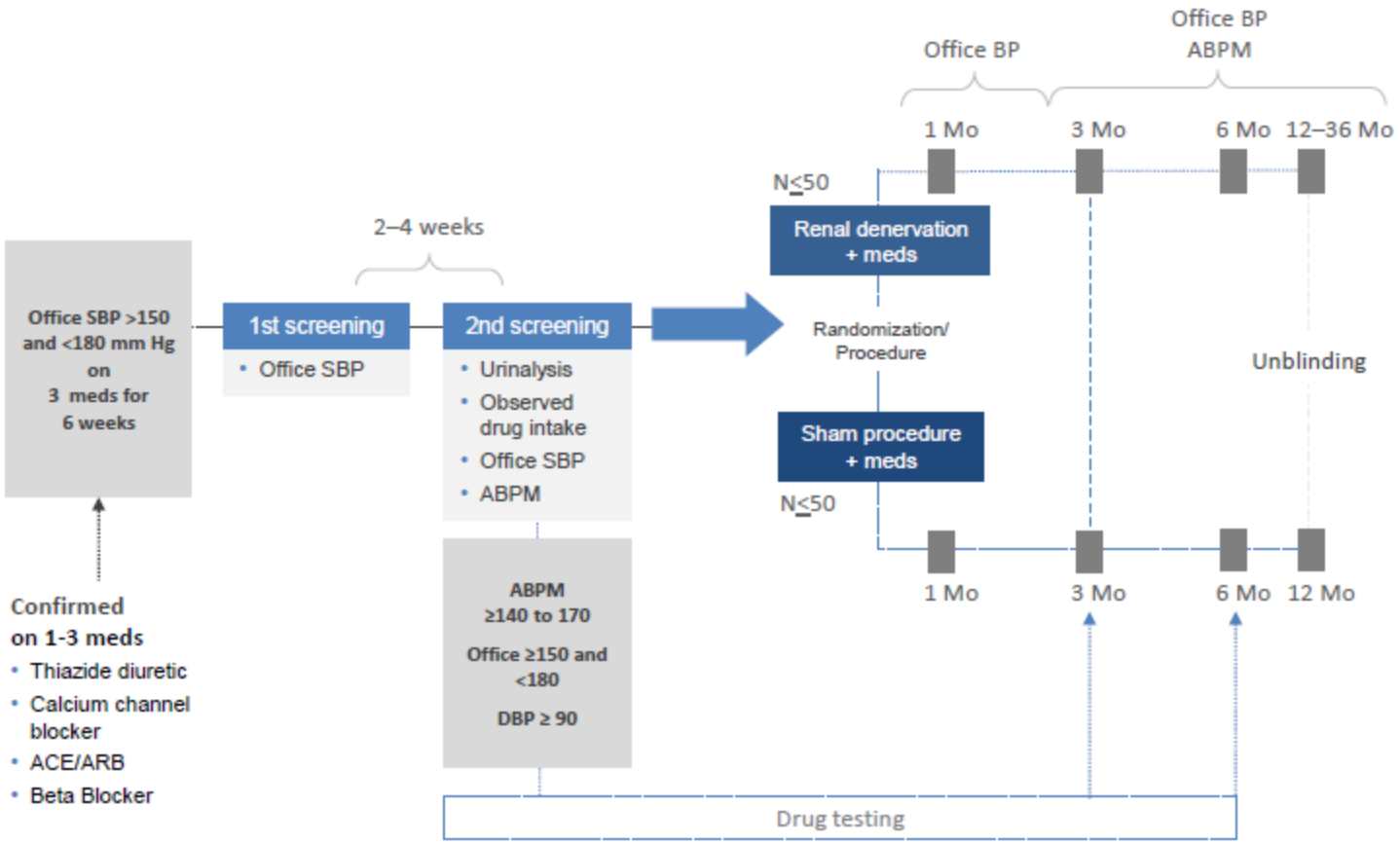
SPYRAL HTN–OFF MED Study



Kandzari et al. Am Heart J 2015

Piedmont HEART

SPYRAL HTN–ON MED Study



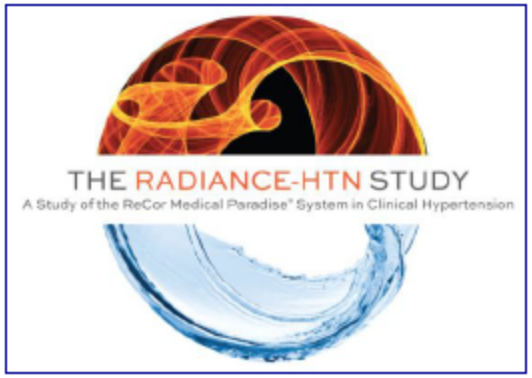
Kandzari et al. Am Heart J 2015

Piedmont HEART

BRIGHAM AND WOMEN'S HOSPITAL

Baim Institute for Clinical Research

RADIANCE-HTN: Randomized, Sham-Controlled Clinical Study: Paradise Ultrasound Renal Denervation System



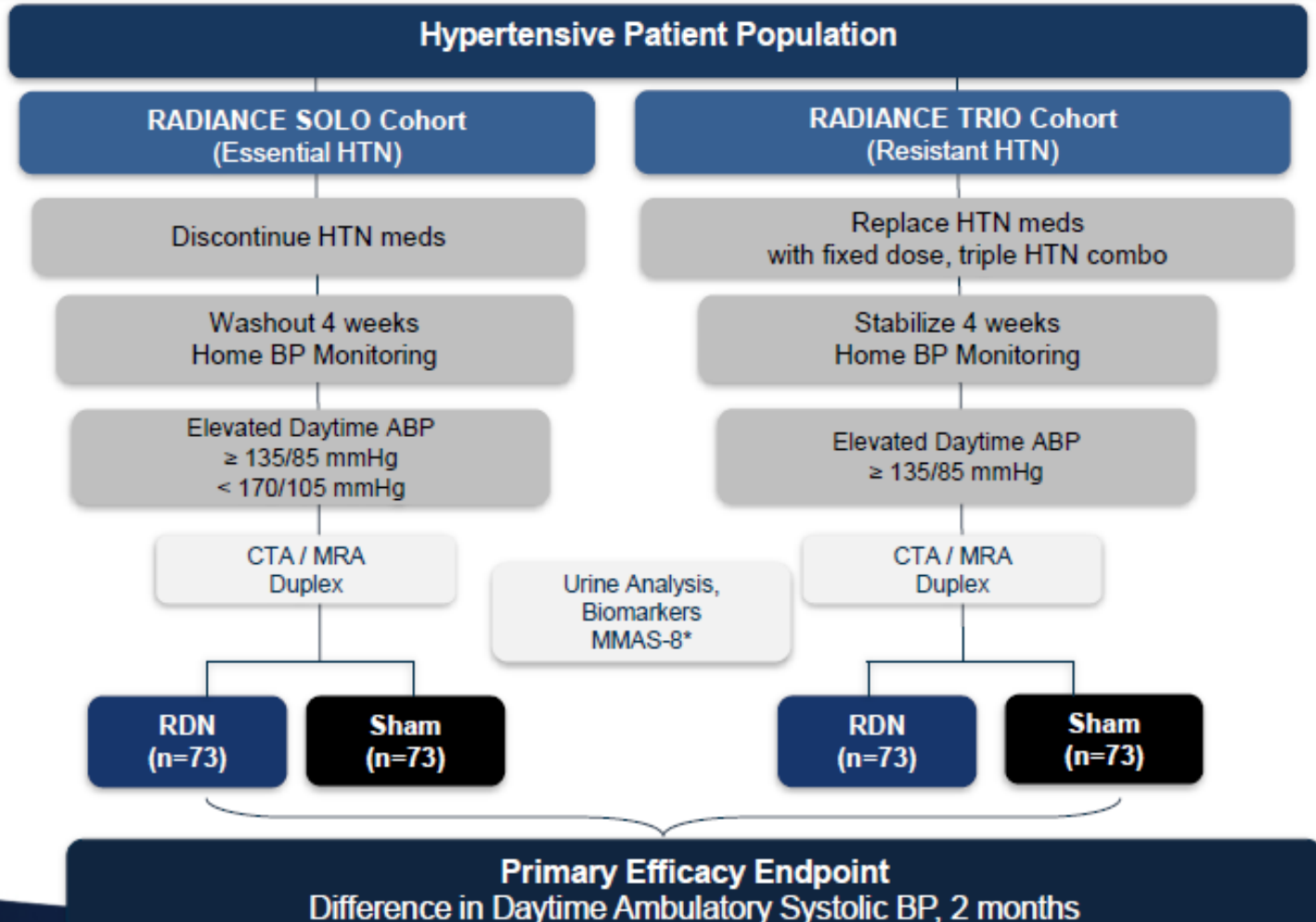
Laura Mauri, MD, MSc

Brigham and Women's Hospital

Professor of Medicine, Harvard Medical School

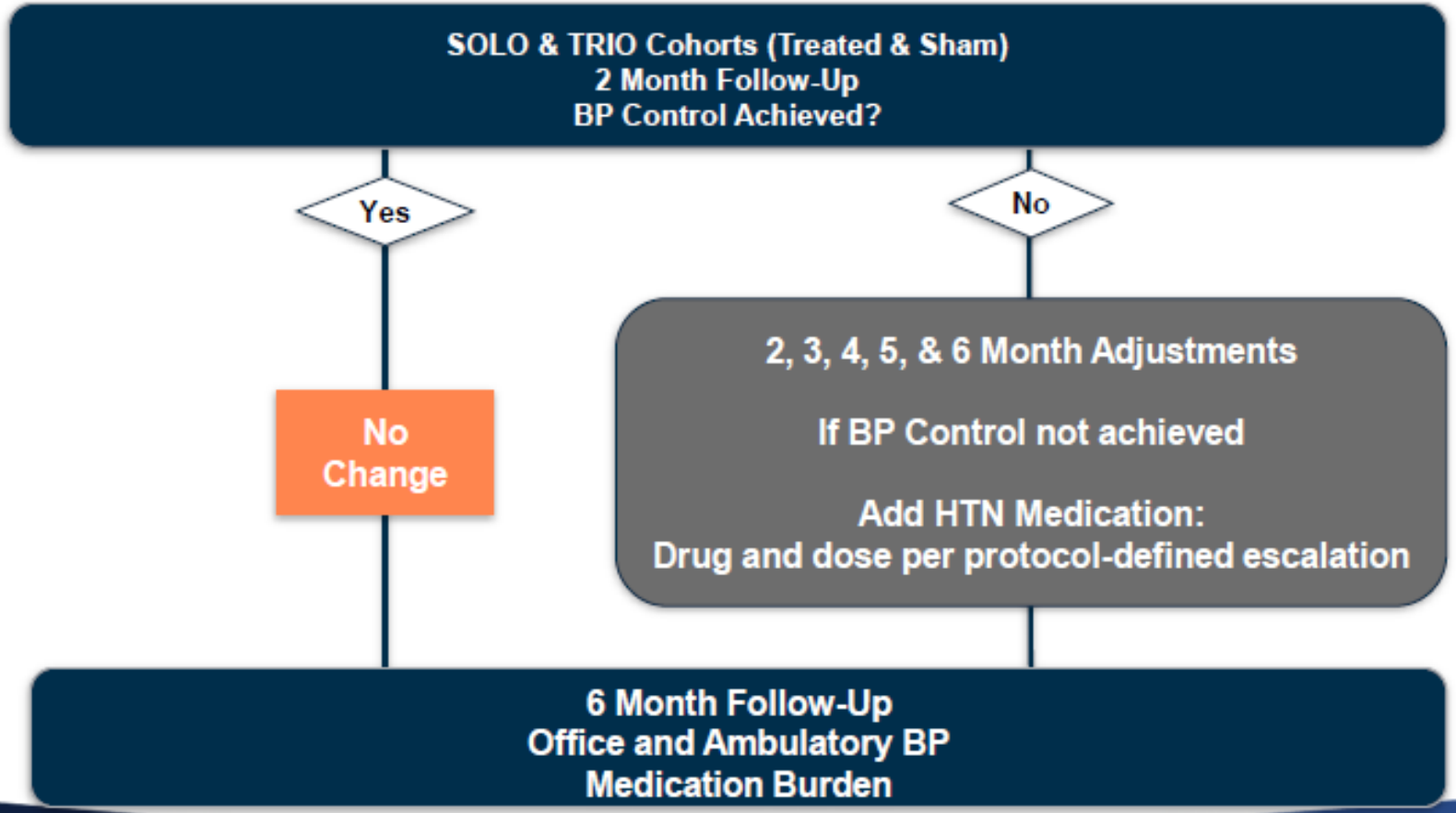
Chief Scientific Officer, Baim Institute for Clinical Research

RADIANCE-HTN Study Overview:



RADIANCE-HTN: Medication Escalation Protocol

Objective: Pre-defined medication adjustment between 2 and 6 months to achieve BP control for all randomized subjects



RADIANCE-HTN Key Patient Eligibility Criteria

Solo Cohort

- Essential HTN on ≤2 HTN meds
- OPB < 180/110mmHg while on 1-2 meds
- or OBP ≥ 140/90 and <180/110mmHg while on no meds
- 4-weeks off meds
- Daytime ABP≥ 135/85mmHg and <170/105mmHg
- No history of CVA
- No repeat hospitalization for hypertensive crisis within prior 12 months

Trio Cohort

- Resistant HTN on≥3 HTN meds, including diuretic
- OBP ≥ 140/90 while on stable regimen of > 3 meds
- 4-week stabilization on single pill, fixed dose, triple medication
- Daytime ABP ≥ 135/85mmHg
- No history of CVA within 3 months
- No documented evidence of secondary hypertension

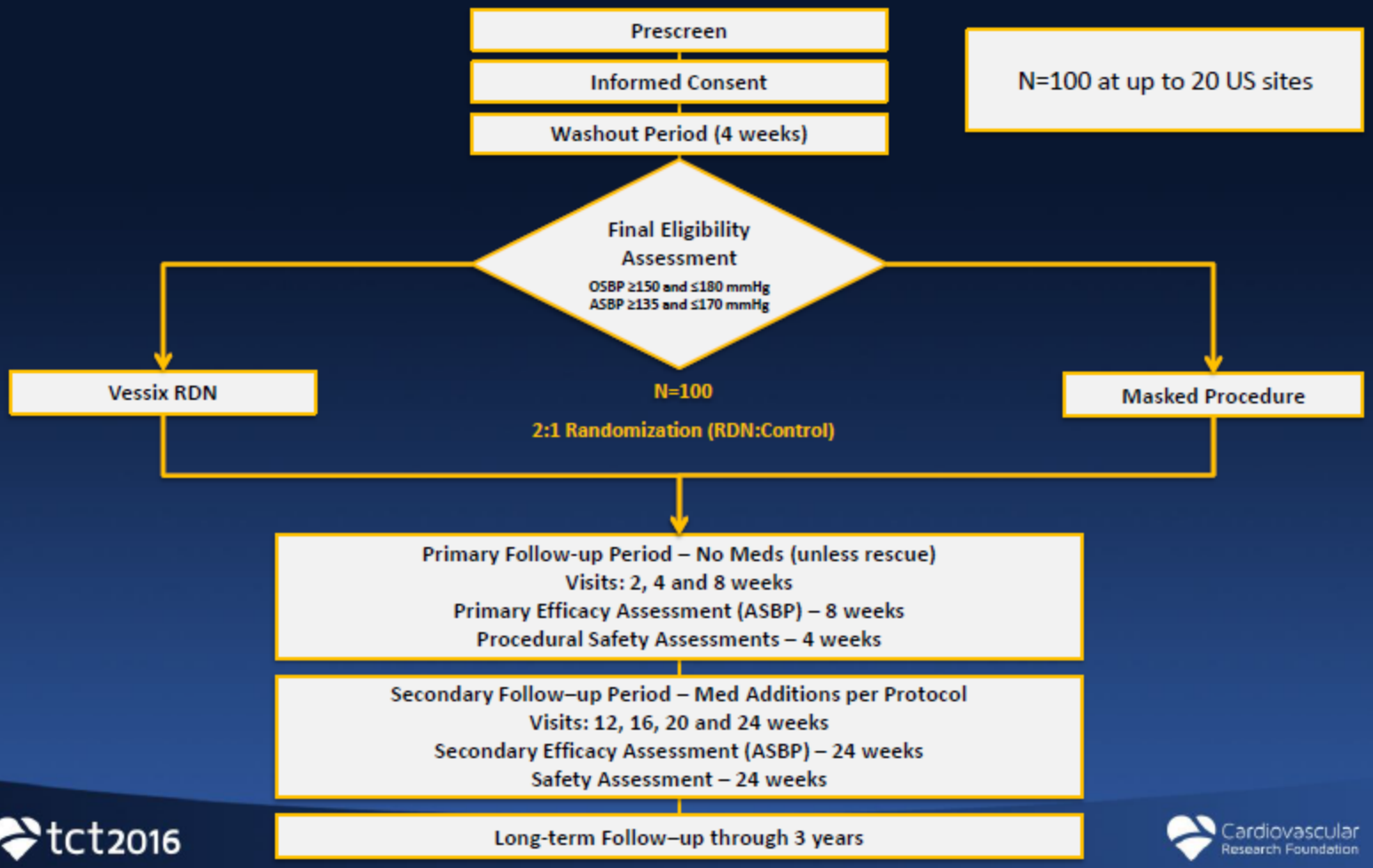
Study Implementation

- 42 sites
- US, UK, Germany, France and the Netherlands
- Enrollment on-going

REDUCE -HTN

REDUCE-HTN: REINFORCE

Study Overview



tct2016

Cardiovascular Research Foundation

REDUCE -HTN

- 6 AYLIK TAKİP
  - ORT 24,5/10,3 mmHg DÜŞÜŞ (N:143 HASTA)
- 18 AYLIK TAKİPTE
  - ORT 30,2/12,7 mm Hg düşüş (N:51 HASTA)

Sievert H, Schofer J, Ormiston J, Hope UC, Meredith IT, Walters DL, Azizi M, Diaz-Cartelle J, Cohen-Mazor M. Renal denervation with a percutaneous bipolar radiofrequency balloon catheter in patients with hypertension: 6-month results from the REDUCE-HTN clinical study. *Eurointervention* 2015;10:1213-20

REINFORCE Study Details

REDUCE-HTN: REINFORCE	
Randomization	2:1 (Test:Control) • Test: Renal Denervation • Control: Masked Procedure (renal angiogram)
Key Inclusion Criteria	• ≥18 and ≤75 • OSBP ≥150 mmHg and ≤180 mmHg based on an average of 3 office-based blood pressure measurements • Avg 24-hour ASBP ≥135 mmHg and ≤170 mmHg • For each kidney, a main renal artery, with or without accessory renal arteries, with diameter ≥3.0 mm and ≤7.0 mm and length ≥20.0 mm
Primary Efficacy Assessment	Mean reduction in average 24-hour ambulatory systolic blood pressure (ASBP) at 8 weeks post randomization

Boston Scientific Renal Denervation

RELIEVE Clinical Series

Vessix Global Clinical Program
RELIEVE

RELIEVE Clinical Series
European Investigator Sponsored Research Collaboration for expanded disease states

Kidney Disease

Renal Denervation - Chronic Kidney Disease
Prospective, single-center RCT, 1:1 - 20pts
Status – Enrolling

Heart Failure

IMPROVE-HF
Prospective, randomized, 1:1 – 70pts
Status - Enrolling

HTN with Comorbidities

REDUCE-CAD – HTN with CHF, AF, or Diabetes
Prospective, observation study – 100 pts
Status – Enrolling

Testing RDN success

How to test success of a RDN
Prospective, single-center, observation – 20 pts
Status - Enrolling

Conclusions

- The REDUCE-HTN: REINFORCE randomized trial is a novel study designed to isolate the effects of renal denervation as a sole treatment for HTN
- Patient recruitment, screening and randomization are currently ongoing
  - Various forms of outreach are being utilized to accelerate recruitment
- The Vessix RELIEVE clinical series is designed to better understand the effects of renal denervation on HTN and other conditions potentially treated with renal denervation

Device Overview and Ongoing Study Design:
St. Jude Medical's EnligHTN Program

William B. White, MD

Professor, Calhoun Cardiology Center
University of Connecticut School of Medicine, Farmington, CT, USA

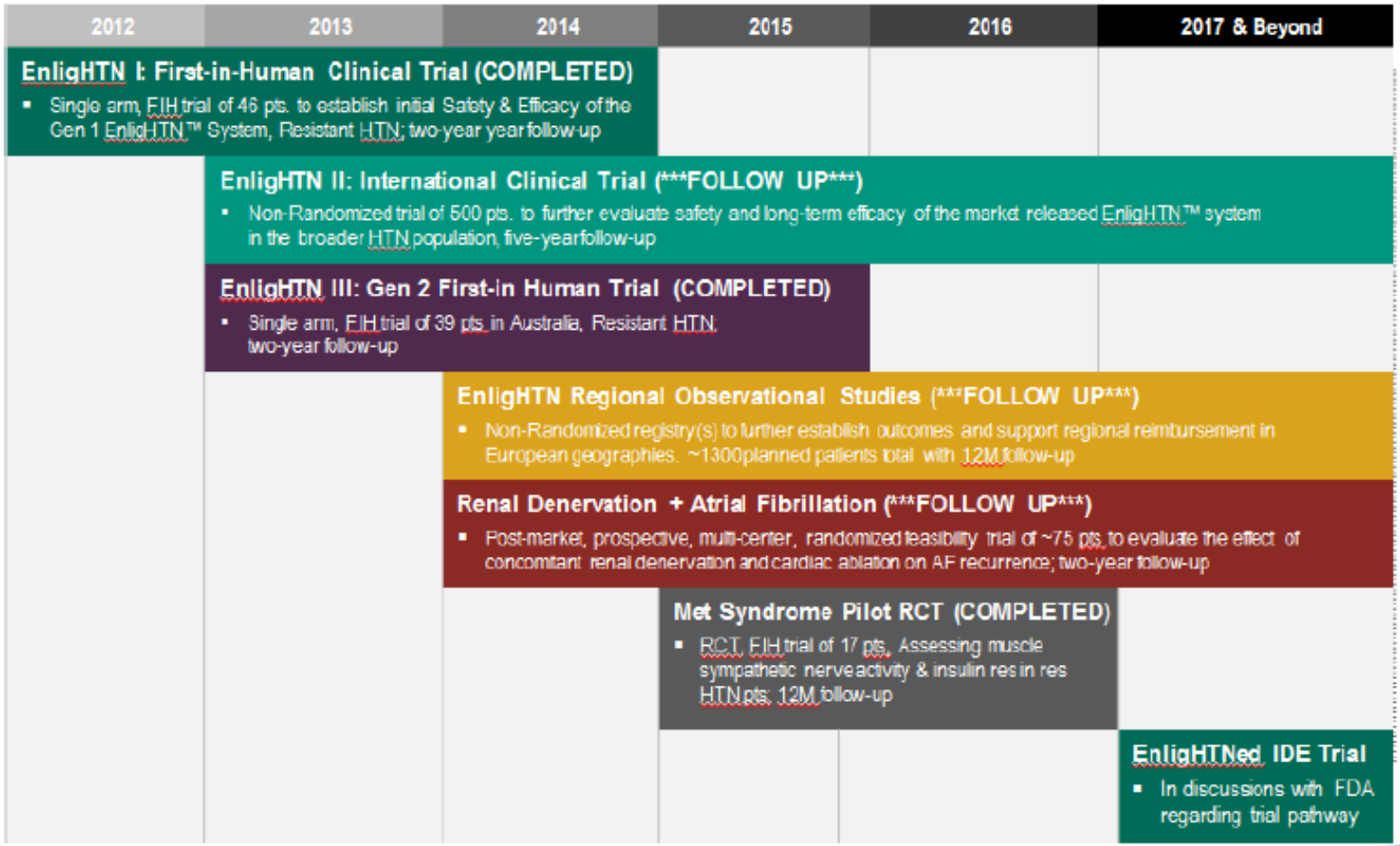
ENLIGHTNED
GLOBAL IDE TRIAL

Steering Committee Members*

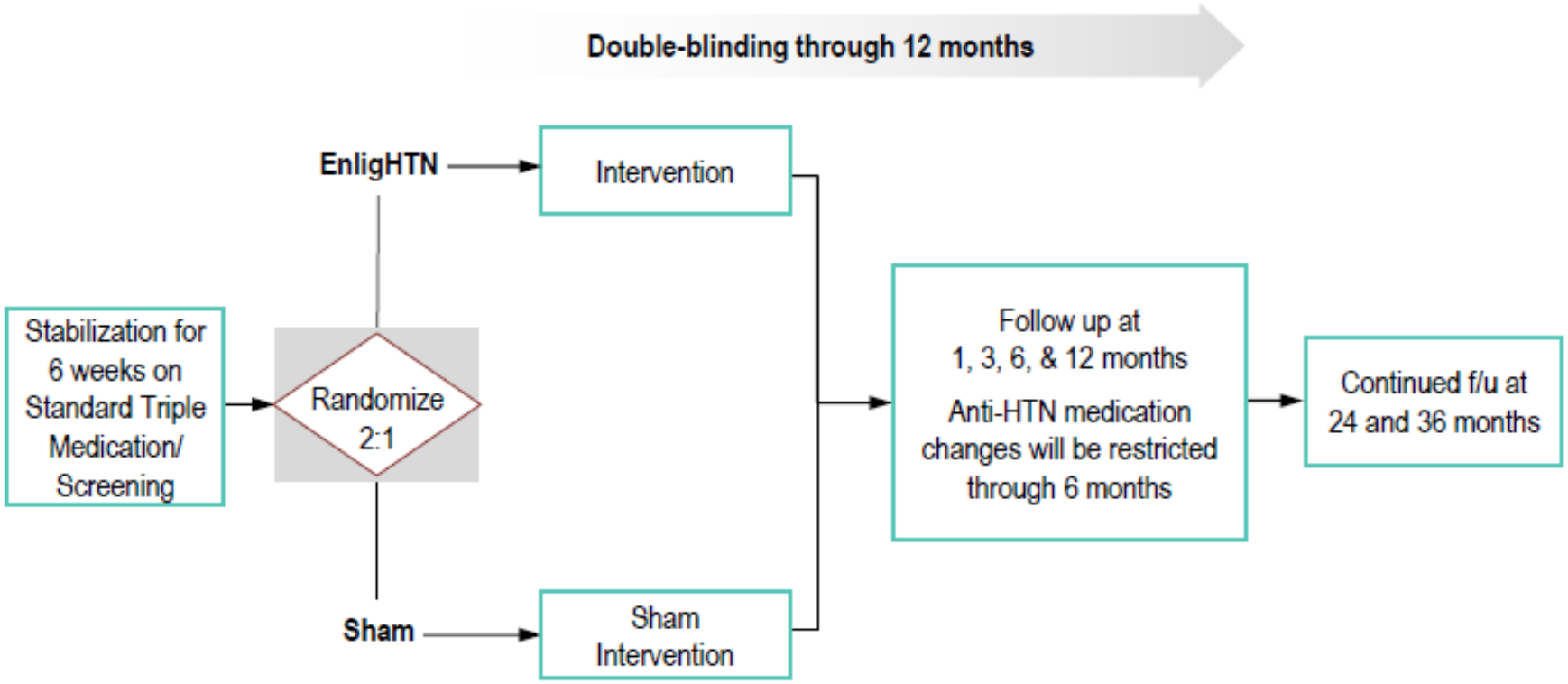
- **Study Chairs:**
  - Felix Mahfoud (Germany) and William B White (USA)
- **Members:**
  - William Gray (USA), Atul Pathak (France), Costas Tsioufis (Greece), and Stephen Worthley (Australia)

*Expertise in Device Therapy, General and Interventional Cardiology, Hypertension and Clinical Pharmacology, Clinical Trials

Ongoing EnligHTN™ Clinical Evidence Series

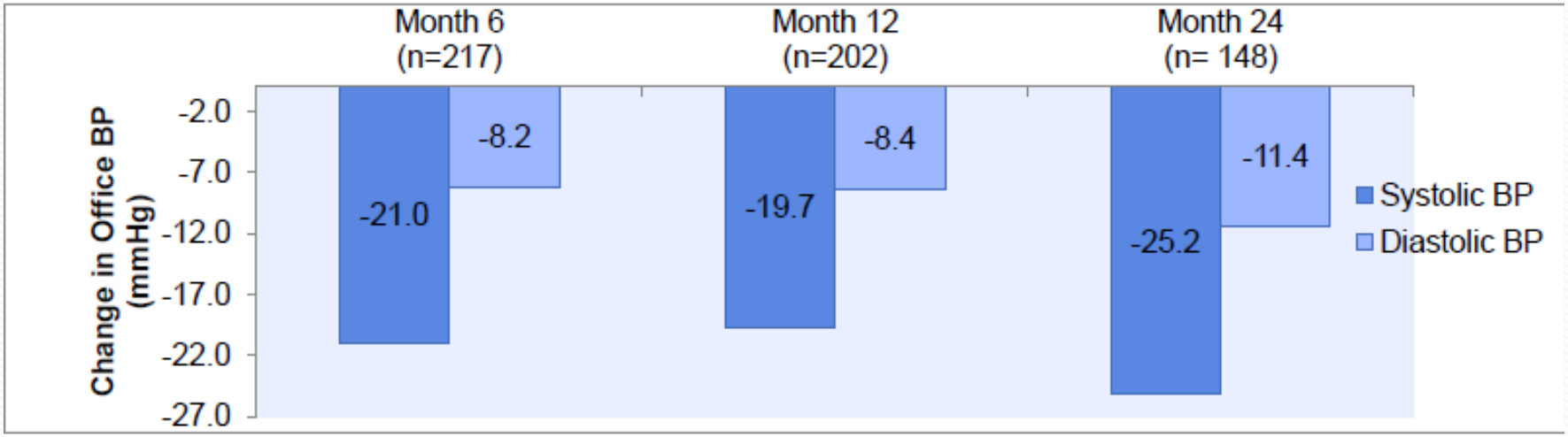


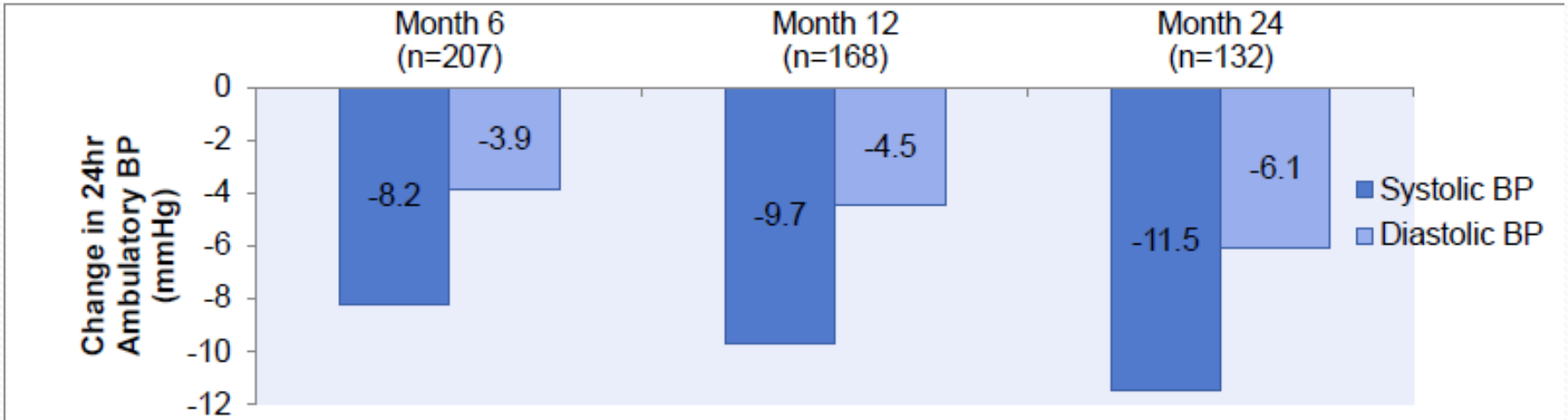
Trial Flow Overview



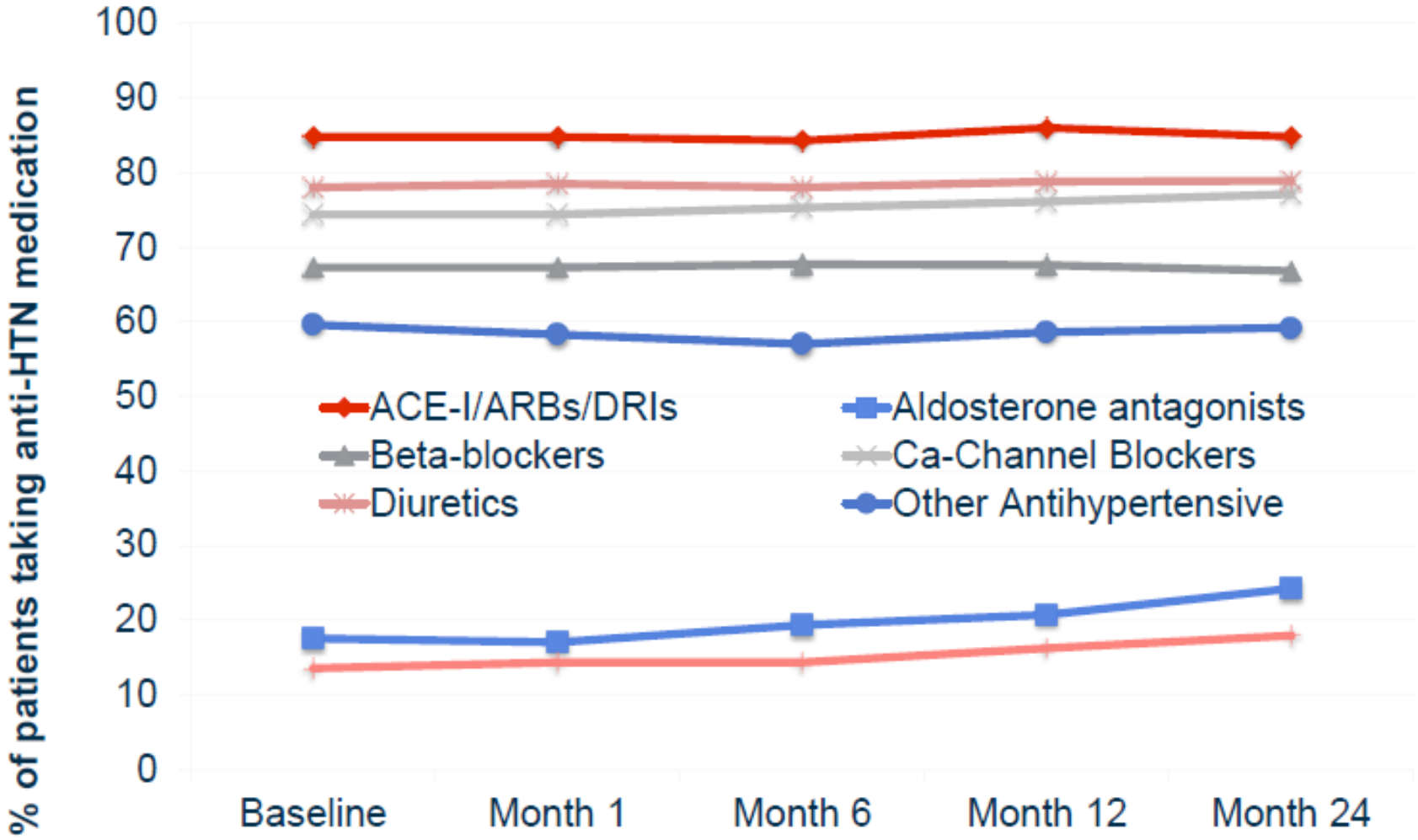
Blood Pressure Reductions through 24 months

(all p values <0.0001)





Importantly, Antihypertensive Medications Were Minimally Altered



- David Kandzari “Thereafter, I do believe that renal denervation would find a common role in the treatment of treatment-resistant hypertension, . . . but we’re still years from that being a reality,” he said.